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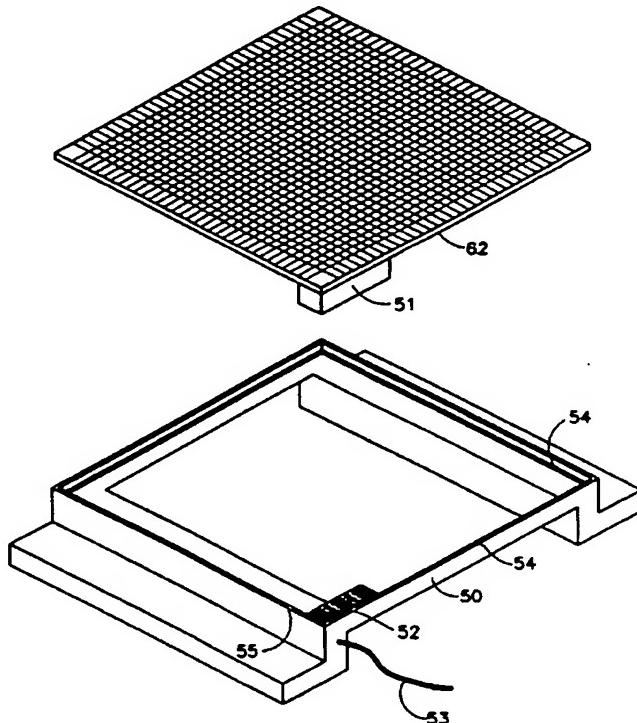
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(54) Title: IMPEDANCE IMAGING DEVICES AND MULTI-ELEMENT PROBE



(57) Abstract

A multi-element probe for providing an electrical connection to a tissue surface comprising: a plurality of individual conductive sensing elements (62), each having a front portion suitable for contact with the tissue surface, a plurality of conductive elements (51, 52) providing an electrical connection to the respective individual sensing elements and a partition or spacing separating the individual sensing elements such that when the individual probes contact the tissue surface they are substantially isolated from each other.

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IMPEDANCE IMAGING DEVICES AND MULTI-ELEMENT PROBE

1

2 FIELD OF THE INVENTION

3 The present invention relates to systems for imaging
4 based on the measurement of electrical potentials at an
5 array of points, especially on the skin or other tissue
6 surface of a patient.

7 BACKGROUND OF THE INVENTION

8 The measurement of electrical potentials on the skin
9 has many uses. For example, electrocardiograms are derived
10 from measuring the potential generated by the heart of a
11 patient at various points on the skin.

12 Skin potentials are also measured in apparatus for
13 determining the electrical impedance of human tissue,
14 including two-dimensional (e.g., U.S. Patents 5,063,937,
15 4,291,708 and 4,458,694) or three-dimensional (e.g., U.S.
16 Patents 4,617,939 and 4,539,640) mapping of the tissue
17 impedance of the body. In such systems an electrical
18 potential is introduced at a point or points on the body and
19 measured at other points at the body. Based on these
20 measurements and on algorithms which have been developed
21 over the past several decades, an impedance map or other
22 indication of variations in impedance can be generated.

23 U.S. Patents 4,291,708 and 4,458,694 and "Breast Cancer
24 screening by impedance measurements" by G. Piperno et al.
25 *Fontiers Med. Biol. Eng.*, Vol. 2, No. 2, pp 111-117, the
26 disclosures of which are incorporated herein by reference,
27 describe systems in which the impedance between a point on
28 the surface of the skin and some reference point on the body
29 of a patient is determined. These references describe the
30 use of a multi-element probe for the detection of cancer,
31 especially breast cancer, utilizing detected variations of
32 impedance in the breast.

33 In these references a multi-element probe is described
34 in which a series of flat, stainless steel, sensing elements
35 are mounted onto a PVC base. A lead wire is connected
36 between each of these elements and detector circuitry. Based

1 on the impedance measured between the elements and a remote
2 part of the body, signal processing circuitry determines the
3 impedance variations in the breast. Based on the impedance
4 determination, tumors, and especially malignant tumors, can
5 be detected.

6 The multi-element probe is a critical component in this
7 system and in other systems which use such probes. On one
8 hand the individual elements must make good contact with the
9 skin and with the corresponding points on the sensing or
10 processing electronics while also being well isolated from
11 each other. On the other hand, use of gels to improve skin
12 contact carries the risk of cross-talk, dried gel build-up
13 on the elements and inter-patient hygienic concerns.

14 A paper titled "Capacitive Sensors for IN-Vivo
15 Measurements of the Dielectric Properties of Biological
16 materials" by Karunayake P.A.P. Esselle and Stanislaw S.
17 Stuchly (IEEE Trans. Inst & Meas. Vol. 37, No. 1, p. 101-
18 105) describes a single element probe for the measurement of
19 in vivo and in vitro measurements of the dielectric
20 properties of biological substances at radio and microwave
21 frequencies. The sensor which is described is not suitable
22 for impedance imaging.

23 A paper entitled "Messung der elektrischen Impedance
24 von Organen- Apparative Ausrüstung für Forschung und
25 klinische Anwendung" by E. Gersing (Biomed. Technik 36
26 (1991), 6-11) describes a system which uses single element
27 impedance probes for the measurement of the impedance of an
28 organ. The device described is not suitable for impedance
29 imaging.

30 A Paper titled "MESURE DE L'IMPEDANCE DES TISSUS
31 HEPATIQUELES TRANSFORMES PAS DES PROCESSUS LESIONELS" by J.
32 Vrana et al. (Ann. Gastroentreol. Hepatol., 1992, 28, no. 4,
33 165-168) describes a probe for assessing deep tissue by use
34 of a thin injection electrode. The electrode was positioned
35 by ultrasound and specimens were taken for cytological and
36 histological assessment. The electrode was constituted on a

1 biopsy needle used to take the samples.

2 A paper titled "Continuous impedance monitoring during
3 CT-guided stereotactic surgery: relative value in cystic and
4 solid lesions" by V. Rajshekhar (British Journal of
5 Neurosurgery (1992) 6, 439-444) describes using an impedance
6 probe having a single electrode to measure the impedance
7 characteristics of lesions. The objective of the study was
8 to use the measurements made in the lesions to determine the
9 extent of the lesions and to localize the lesions more
10 accurately. The probe is guided to the tumor by CT and four
11 measurements were made within the lesion as the probe passed
12 through the lesion. A biopsy of the lesion was performed
13 using the outer sheath of the probe as a guide to position,
14 after the probe itself was withdrawn.

15 A paper titled "Rigid and Flexible Thin-Film Multi-
16 electrode Arrays for Transmural Cardiac Recording" by J. J.
17 Mastrototaro et al. (IEEE TRANS. BIOMED. ENG. Vol. 39, No.
18 3, March 1992, 271-279) describes a needle probe and a flat
19 probe each having a plurality of electrodes for the
20 measurement of electrical signals generated in the heart.

21 A paper entitled "Image-Based Display of Activation
22 Patterns Derived from Scattered Electrodes" by D. S. Buckles
23 et al. (IEEE TRANS. BIOMED ENGR. Vol. 42, No. 1, January
24 1995, 111-115) describes a system for measurement of
25 electrical signals generated on the heart by use of an array
26 of electrodes on a substrate. The heart with the electrodes
27 in place is viewed by a TV camera and an operator marks the
28 positions of the electrodes on a display. The system then
29 displays the heart (as visualized prior to the placement of
30 the electrodes) with the position markings.

31 A paper entitled "Development of a Multiple Thin-Film
32 Semimicro DC-Probe for Intracerebral Recordings" by G. A.
33 Urban et al. (IEEE TRANS. BIOMED ENGR. Vol. 37, No. 10,
34 October 1990, 913-917) describes an elongate alumina ceramic
35 probe having a series of electrodes along its length and
36 circumference for measuring functional parameters

1 (electrical signals) in the brain. Electrophysiological
2 recording, together with electrosimulation at the target
3 point during stereotactic surgery, was performed in order to
4 ensure exact positioning of the probe after stereotactic
5 calculation of the target point. Bidimensional X-Ray imaging
6 was used in order to verify the exact positioning of the
7 electrode tip.

8 SUMMARY OF THE INVENTION

9 It is an object of certain aspects of the invention to
10 provide a multi-element probe having improved and more
11 uniform and repeatable contact with the skin with minimal
12 operator expertise and minimal risk of cross-patient
13 contamination.

14 It is an object of certain aspects of the invention to
15 provide improved inter-element electrical isolation, and to
16 permit sliding of the probe while it is urged against the
17 skin.

18 It is an object of certain aspects of the invention to
19 provide a relatively inexpensive disposable multi-element
20 probe.

21 It is an object of certain aspects of the invention to
22 provide a multi-element probe having sufficient transparency
23 to allow for viewing of tissue surface features and to allow
24 for referencing the probe with respect to physical features
25 of or on the skin.

26 It is an object of certain aspects of the invention to
27 provide a method of distinguishing between artifacts and
28 abnormalities.

29 It is an object of certain aspects of the invention to
30 provide a system for electrical impedance imaging which
31 simultaneously acquires, uses and preferably displays both
32 capacitance and conductance information.

33 It is an object of certain aspects of the invention to
34 provide a system for electrical impedance testing of the
35 breast or other body region which provides more accurate
36 information regarding the position of impedance

1 abnormalities detected in the breast or other region.

2 It is an object of certain aspects of the invention to
3 provide for electrical impedance testing with a variable
4 spatial resolution.

5 It is an object of certain aspects of the invention to
6 provide for two dimensional electrical impedance testing
7 giving an indication of the distance of an abnormality from
8 the surface of the skin.

9 It is an object of certain aspects of the invention to
10 provide apparatus especially suitable for breast impedance
11 measurements.

12 It is an object of certain aspects of the invention to
13 provide guidance for placement of elongate objects such as
14 biopsy needles, localization needles, fiber optic endoscopes
15 and the like using real time and/or recorded stereotactic
16 images to guide the object.

17 It is a further object of certain aspects of the invention to
18 provide a biopsy needle having an impedance
19 measuring function to aid in the taking of a biopsy.

20 It is an object of certain aspects of the invention to
21 provide more direct comparison between the results of
22 electrical impedance maps and the results of optical,
23 ultrasound or other imaging modalities.

24 It is an object of certain aspects of the invention to
25 provide apparatus and method for indicating, on an
26 anatomical illustration, the location and region from which
27 an impedance image, shown together with the illustration is
28 derived.

29 It is an object of certain aspects of the invention to
30 provide apparatus which facilitates direct comparison
31 between X-Ray and impedance mammographic images, as for
32 example by superposition of the images.

33 It is an object of certain aspects of the invention to
34 provide a method of determining a multi-frequency impedance
35 map.

36 It is an object of certain aspects of the invention to

1 optimize the impedance mapping utilizing a pulsed voltage
2 excitation.

3 It is an object of certain aspects of the invention to
4 provide palpation and tactile sensing of an area while
5 simultaneously providing an impedance image of the area.

6 In general, the term "skin" as used herein means the
7 skin or other tissue of a subject.

8 There is therefore provided, in accordance with a
9 preferred embodiment of the invention, a multi-element probe
10 for providing an electrical connection to a tissue surface,
11 comprising:

12 a plurality of individual conductive sensing elements,
13 each having a front portion suitable for contact with the
14 tissue surface;

15 a plurality of conductive elements providing an
16 electrical connection to the respective individual sensing
17 elements; and

18 a partition separating the individual sensing elements
19 such that, when the sensing elements contact the tissue
20 surface, the sensing elements are substantially electrically
21 isolated from each other.

22 Preferably, the sensing elements comprise a conductive,
23 viscous gel. Alternatively or additionally, in a preferred
24 embodiment of the invention, the sensing elements comprise a
25 conductive, flexible, solid.

26 Alternatively or additionally, in a preferred
27 embodiment of the invention the sensing elements comprise a
28 sponge impregnated with a conductive viscous gel.

29 In a preferred embodiment of the invention, each
30 individual sensing element is located in a well formed by
31 the partition and a substrate underlying the sensing
32 element.

33 Preferably, the side of the substrate opposite the
34 sensing elements is formed with indentations for aligning
35 the multi-element probe.

36 In a preferred embodiment of the invention, the well is

1 formed by embossing the partition on a sheet of material,
2 whereby the un-embossed portion of the sheet forms the
3 substrate underlying the sensing element. Preferably, the
4 indentations are the back of the embossed wells.

5 In an alternative preferred embodiment of the
6 invention, the well is formed by laminating a grid formed by
7 holes punched in a sheet or formed by extrusion to the
8 substrate.

9 Alternatively, the well is formed by printing the
10 partitions onto the substrate.

11 In a preferred embodiment of the invention, there is an
12 electrical connection between a first surface of the
13 substrate inside the well and a second, opposite, surface of
14 the substrate. Preferably the apparatus also comprises an
15 anisotropic conductive sheet overlying the second surface of
16 the substrate.

17 Alternatively the probe preferably comprises a
18 conductive contact on the second surface of the substrate
19 which is electrically connected to the first surface of the
20 substrate and an adhesive contact overlying the conductive
21 contact.

22 In a preferred embodiment of the invention, the sensing
23 elements do not extend past the top of the partition or do
24 not extend to the top of the partition.

25 In a preferred embodiment of the invention the probe
26 includes a cover having a conductive surface facing the
27 front portion of the sensing elements.

28 There is further provided in accordance with a
29 preferred embodiment of the invention, a multi-element probe
30 for providing an electrical connection to tissue,
31 comprising:

32 a plurality of individual conductive sensing elements,
33 each having a front portion suitable for contact with the
34 tissue;

35 a plurality of conductive elements providing an
36 electrical connection to the respective individual sensing

1 elements; and

2 a cover having a surface facing the front portion of
3 the sensing elements, at least that portion of said surface
4 facing the sensing elements being an electrically conductive
5 surface.

6 Preferably, the cover is formed of a flexible material
7 and wherein, in an unstressed position said electrical
8 conductive surface does not contact said conductive sensing
9 elements. In a preferred embodiment of the invention, the
10 cover is so configured that the surface contacts the sensing
11 elements when a surface of the cover opposite the conductive
12 surface is pressed toward the sensing elements.

13 In a preferred embodiment of the invention, the cover
14 also includes an area, on the surface facing the individual
15 sensing elements, remote from the individual sensing
16 elements, which is a conductive area electrically connected
17 to said portions facing the sensing elements, the multi-
18 element probe also including a contact electrically
19 connected to the exterior of the probe. Preferably, in an
20 unstressed position said electrical conductive surface does
21 not contact said contact and wherein said cover is so
22 configured that the conductive area contacts the contact
23 when a surface of the cover opposite the conductive surface
24 is pressed toward the sensing elements.

25 In a preferred embodiment of the invention the probe
26 comprises at least one contact suitable for connection to an
27 external source of electrical energy and also including
28 impedance elements between the conductive surfaces opposite
29 the sensing elements and the contact.

30 Preferably the cover includes impedance elements
31 between the conductive surfaces opposite the sensing
32 elements and the contact.

33 There is further provided, in accordance with a
34 preferred embodiment of the invention, a multi-element probe
35 for providing an electrical connection to a tissue surface
36 comprising:

1 a plurality of individual conductive sensing elements,
2 each having a front portion suitable for contact with the
3 tissue surface; and

4 a plurality of conductive elements providing an
5 electrical connection to the respective individual sensing
6 elements,

7 wherein the side of the substrate opposite the sensing
8 elements is formed with indentations for aligning multi-
9 element probe.

10 There is further provided, in accordance with a
11 preferred embodiment of the invention, a multi-element probe
12 for the measurement of impedance of tissue, wherein the
13 elements of the probe are sufficiently transparent to allow
14 visualization of tissues beneath the probe when the probe is
15 place in contact with the tissues.

16 There is further provided, in accordance with a
17 preferred embodiment of the invention, a multi-element probe
18 for providing an electrical connection to a tissue surface
19 comprising:

20 a plurality of individual conductive sensing elements,
21 each having a front portion suitable for contact with the
22 tissue surface; and

23 a plurality of conductive elements providing an
24 electrical connection to the respective individual sensing
25 elements, wherein

26 the elements of the probe are sufficiently transparent
27 to allow visualization of tissues beneath the probe when the
28 probe is place in contact with the tissues.

29 Preferably, the sensing elements are formed of a spongy
30 conductive material.

31 There is further provided, in accordance with a
32 preferred embodiment of the invention a multi-element probe
33 for providing an electrical connection to a tissue surface
34 comprising:

35 a plurality of individual conductive sensing elements,
36 each having a front portion suitable for contact with the

1 tissue surface; and

2 a plurality of conductive elements providing an
3 electrical connection to the respective individual sensing
4 elements,

5 wherein the sensing elements are formed of a spongy
6 conductive material.

7 Preferably, the sensing elements are formed on a
8 flexible surface, whereby the multi-element probe conforms,
9 at least in part, to the tissue.

10 Preferably, the probe is provided with apertures
11 between sensing elements suitable for the passage of a thin
12 elongate object.

13 There is further provided, in accordance with a
14 preferred embodiment of the invention, a multi-element probe
15 for providing an electrical connection to a tissue surface
16 comprising:

17 an array of individual conductive sensing elements
18 spaced over a surface, each element having a front portion
19 suitable for contact with the tissue surface; and

20 a plurality of conductive elements providing an
21 electrical connection to the respective individual sensing
22 elements,

23 wherein the area of the conductive elements comprises
24 less than 50% of the total area encompassed by the array.

25 There is further provided, in accordance with a
26 preferred embodiment of the invention a multi-element probe
27 for providing an electrical connection to a tissue surface
28 comprising:

29 a plurality of individual conductive sensing elements,
30 each having a front portion suitable for contact with the
31 tissue surface; and

32 a plurality of conductive elements providing an
33 electrical connection to the respective individual sensing
34 elements,

35 wherein the probe is provided with apertures between
36 sensing elements suitable for the passage of a thin elongate

1 object.

2 Preferably, at least a portion of the surface of the
3 probe facing the tissue to be measured is adhesive to the
4 tissue.

5 There is further provided, in accordance with a
6 preferred embodiment of the invention a multi-element probe
7 for providing an electrical connection to a tissue surface
8 comprising:

9 a plurality of individual conductive sensing elements,
10 each having a front portion suitable for contact with the
11 tissue surface; and

12 a plurality of conductive elements providing an
13 electrical connection to the respective individual sensing
14 elements,

15 wherein at least a portion of the surface of the probe
16 facing the tissue to be measured is adhesive to the tissue.

17 In a preferred embodiment of the invention, the probe
18 further includes:

19 means for attaching the probe to the finger of a
20 person whereby the person can perform palpative examination
21 concurrently with impedance imaging.

22 There is further provided, in accordance with a
23 preferred embodiment of the invention a multi-element probe
24 for providing an electrical connection to a tissue surface
25 comprising:

26 a plurality of individual conductive sensing elements,
27 each having a front portion suitable for contact with the
28 tissue surface; and

29 a glove having fingers, said sensing elements being
30 attached to the outside of one of the glove at one of the
31 fingers whereby a wearer of the glove can perform palpative
32 examination concurrently with impedance imaging.

33 There is further provided, in accordance with a
34 preferred embodiment of the invention, a multi-element
35 intermediate device for providing an electrical connection
36 between a multiconductor sensor device and a tissue surface

1 comprising a plurality of individual conductive sensing
2 element, electrically insulated from each other, each having
3 a front portion suitable for contact with the tissue surface
4 and a back portion detachably matable to the multi-conductor
5 sensor device.

6 Preferably, the intermediate device includes electrical
7 contacts on the back portion which are electrically
8 connected to the sensing element and which contact a
9 plurality of mating contacts on the multi-conductor sensor
10 device.

11 There is further provided, in accordance with a
12 preferred embodiment of the invention a catheter or
13 endoscopic probe comprising:

14 a multi-element probe as described above; and
15 a fiber optic viewer whose field of view includes at
16 least one surface of the probe when the probe is in contact
17 with the tissue.

18 There is further provided, in accordance with a
19 preferred embodiment of the invention a catheter or
20 endoscopic probe comprising:

21 a multi-element probe for providing an electrical
22 connection to a tissue surface, the probe including a
23 plurality of individual conductive sensing elements on a
24 substrate, each sensing element having a front portion
25 suitable for contact with the tissue surface and fiduciary
26 marks visible from an other surface; and

27 a fiber optic viewer whose field of view includes at
28 least the other surface of the probe.

29 There is further provided, in accordance with a
30 preferred embodiment of the invention a biopsy needle
31 having:

32 a leading end for insertion into tissue to undergo
33 biopsy and an elongated outer surface; and

34 at least one impedance sensing element formed on said
35 outer surface which provides electrical connection to
36 tissue during biopsy.

1 Preferably, the at least one sensing element comprises
2 a plurality of sensing elements electrically insulated from
3 each other and spaced along the length of the outer surface.

4 Alternatively or additionally, the at least one sensing
5 element preferably comprises a plurality of sensing elements
6 electrically insulated from each other and spaced along the
7 circumference of the outer surface.

8 In a preferred embodiment of the invention, at least
9 one sensing element comprises a plurality of sensing
10 elements electrically insulated from each other and forming
11 a matrix of elements spaced along the length and
12 circumference of the outer surface.

13 There is further provided, in accordance with a
14 preferred embodiment of the invention apparatus for
15 impedance imaging of a breast comprising:

16 a multi-element probe comprising a plurality of sensing
17 elements and adapted for mounting on one side of a breast;

18 an electrode adapted for mounting on a side of the
19 breast substantially opposite the multi-element probe; and

20 a source of electrical energy which provides a voltage
21 between at least a portion of the electrode and at least one
22 element of the probe.

23 There is further provided, in accordance with a
24 preferred embodiment of the invention apparatus for
25 impedance imaging of a breast comprising:

26 a multi-element probe comprising a plurality of sensing
27 elements and adapted for mounting on one side of a breast;

28 an electrode adapted for mounting on a side of the
29 breast substantially opposite the multi-element probe;

30 an additional electrode adapted for mounting on portion
31 of the body remote from the breast; and

32 a source of electrical energy which provides a voltage
33 between the additional electrode and at least one element of
34 the probe.

35 Preferably, the multi-element probe and the electrode
36 adapted for mounting on a side of the breast form respective

1 parallel planes.

2 Alternatively, in a preferred embodiment of the
3 invention, the multi-element probe and the electrode adapted
4 for mounting on a side of the breast form two planes at an
5 angle to each other.

6 Preferably, the apparatus includes a plurality of
7 receivers which measure an electrical signal at the sensing
8 elements.

9 In a preferred embodiment of the invention, the
10 electrode is adapted for mounting on a side of the breast
11 comprises a second multi-element probe.

12 Preferably, at least one of the multi-element probes is
13 non-planar to conform to the shape of the breast. The non-
14 planar array can be either rigid or flexible.

15 Alternatively or additionally at least one of the
16 multi-element probes is flexible so as to conform to the
17 shape of the breast.

18 There is further provided, in accordance with a
19 preferred embodiment of the invention, apparatus for
20 impedance imaging of a breast comprising:

21 a first multi-element probe comprising a plurality of
22 sensing elements and adapted for mounting on one side of a
23 breast;

24 a second multi-element probe adapted for mounting on a
25 side of the breast substantially opposite the multi-element
26 probe; and

27 a source of electrical energy which alternatively
28 energizes at least some of the elements of one or the other
29 of the first and second multi-element probes by supplying a
30 voltage thereto, wherein the unenergized one of the multi-
31 element probes forms an image based on the voltage applied
32 to the energized probe.

33 There is further provided, in accordance with a
34 preferred embodiment of the invention apparatus for
35 impedance imaging of tissue comprising:

36 an impedance probe which produces signals

1 representative of impedance values sensed by the elements
2 and having fiduciary marks which are visible when the probe
3 contacts the tissue;

4 an impedance image generator which receives the signals
5 and produces an impedance image;

6 a video camera which views the probe and tissue and
7 generates a video image; and

8 a video image processor which receives a video image of
9 the tissue without the probe in place and an image of the
10 tissue with the probe in place, and provides a video image
11 of the tissue with the fiduciary marks and impedance image
12 superimposed thereon.

13 There is further provided, in accordance with a
14 preferred embodiment of the invention a method of impedance
15 imaging of the breast comprising:

16 (a) positioning a multi-element probe, comprising a
17 plurality of sensing elements, on one side of the breast;

18 (b) positioning an electrode on a side of the breast
19 substantially opposite the multi-element probe;

20 (c) electrifying the electrode; and

21 (d) measuring a signal at at least some of the elements
22 of the multi-element probe.

23 There is further provided, in accordance with a
24 preferred embodiment of the invention a method of impedance
25 imaging of the breast comprising:

26 (a) positioning a multi-element probe, comprising a
27 plurality of sensing elements, on one side of the breast;

28 (b) positioning an electrode on a side of the breast
29 substantially opposite the multi-element probe;

30 (c) positioning a second electrode on a portion of the
31 body;

32 (d) electrifying the second electrode; and

33 (e) measuring a signal at at least some of the elements
34 of the multi-element probe.

35 Preferably (b) comprises positioning a second multi-
36 element probe on a side of the breast substantially opposite

1 the multi-element probe.

2 There is further provided, in accordance with a
3 preferred embodiment of the invention a method of impedance
4 imaging of the breast comprising:

5 positioning a first multi-element probe, comprising a
6 plurality of sensing elements, on one side of the breast;

7 positioning a second multi-element probe on a side of
8 the breast substantially opposite the multi-element probe;

9 electrifying fewer than all of the plurality of
10 sensing elements of the second multi-element probe; and

11 measuring a signal at at least some of the elements of
12 the first multi-element probe.

13 There is further provided, in accordance with a
14 preferred embodiment of the invention a method for guidance
15 in the placement of an elongate element in a region of a
16 subject comprising:

17 (a) inserting the elongate element into tissue, said
18 element including a plurality of impedance measuring sensing
19 elements thereon;

20 (b) measuring the impedance between the plurality of
21 sensing elements and an electrode in contact with the
22 subject; and

23 (c) guiding the element to a desired position having
24 defined impedance properties in response to measurements of
25 impedance made in (b).

26 Preferably the method also includes:

27 imaging the region of the subject including the
28 elongate element and generating an image thereof;

29 receiving the image and the measurements of impedance
30 made in (b) and superimposing a representation of the
31 impedance measurements on the image of the elongate element
32 and surrounding tissues; and

33 displaying said superimposed images.

34 In a preferred embodiment of the invention the outer
35 surface of the elongate element is formed with a matrix of
36 impedance measuring elements each measuring the tissue

1 impedance in a direction generally perpendicular to the
2 element and the display indicates a guiding direction for
3 the elongate element based on the impedance measurements.

4 There is further provided, in accordance with a
5 preferred embodiment of the invention, a method for guidance
6 in the placement of an elongate element in portion of a
7 patient comprising:

8 forming a first two-dimensional impedance image of at
9 least a part of said portion from a given direction;

10 forming second a two dimensional impedance image of at
11 least a part of the portion using a multi-element impedance
12 probe placed at a known angle to the plane of the first
13 image;

14 inserting the elongate element between elements of the
15 multi-element probe; and

16 guiding the elongate element to a point at which a
17 biopsy is to be taken at least partially under the guidance
18 of the first and second two dimensional images.

19 Preferably, the elongate element is inserted into the
20 body through a hole in an array of impedance probe elements
21 and including:

22 providing a two-dimensional impedance image based on
23 signals received by the array;

24 guiding the elongate element based on the two-
25 dimensional image; and

26 determining the desired depth of the elongate element
27 based on impedance signals received from the impedance
28 measuring elements on the elongate element.

29 There is further provided, in accordance with a
30 preferred embodiment of the invention, a method comprising:

31 providing an impedance measurement system including a
32 multi-element probe attached to at least one finger of an
33 examiner; and

34 providing an indication of impedance which is generated
35 on the basis of signals detected by said elements, whereby
36 both a tactile and impedance indication of tissue being

1 examined are simultaneously acquired.

2 There is further provided, in accordance with a
3 preferred embodiment of the invention, a method for
4 improving the sensitivity of impedance imaging comprising:
5 contacting tissue with a multi-element probe;
6 contacting a different portion of tissue with at least
7 one electrode;

8 exciting the at least one electrode with a pulsed
9 voltage;

10 measuring signals, responsive to said pulsed voltage at
11 at least a plurality of the elements of the probe;

12 computing the real and imaginary parts of an admittance
13 represented by said voltage and signals for a plurality of
14 frequencies at a plurality of said elements; and

15 choosing at least one frequency as a measurement
16 frequency which gives a large difference for said measures
17 at selected different elements of the probe.

18 There is further provided, in accordance with a
19 preferred embodiment of the invention, a method for
20 identifying, in a multi-element impedance probe which forms
21 an impedance map of tissue when placed on the surface
22 thereof, artifacts among impedance deviations from the
23 surroundings, the method comprising:

24 manipulating the tissue underlying the probe while the
25 probe remains in stationary contact with the surface of the
26 tissue; and

27 identifying as a non-artifact those impedance
28 deviations which shift in the direction of the manipulation
29 on the impedance map.

30 There is further provided, in accordance with a
31 preferred embodiment of the invention, a method for
32 identifying, in a multi-element impedance probe which forms
33 an impedance map of tissue when placed on the surface
34 thereof, artifacts among impedance deviations from the
35 surroundings, the method comprising:

36 moving the probe along the surface of the tissue; and

1 identifying as an artifact those impedance deviations
2 which remain stationary or disappear in the impedance map
3 when the probe is moved.

4 There is further provided, in accordance with a
5 preferred embodiment of the invention, a method for
6 identifying, in a multi-element impedance probe which forms
7 an impedance map of tissue when placed on the surface
8 thereof, artifacts among impedance deviations from the
9 surroundings, the method comprising:

10 moving the probe together with the tissue; and
11 identifying as a fixed artifact those impedance
12 deviations which move on the impedance map, in the opposite
13 direction from the movement of the probe and the tissue.

14 There is further provided, in accordance with a
15 preferred embodiment of the invention, a method of
16 displaying impedance imaging information comprising:

17 displaying at least one impedance image of a region;
18 and

19 displaying an indication of the imaged region on a
20 representation of the physiology of the patient.

21 Preferably the display method includes:

22 simultaneously displaying both a capacitance and a
23 conductance map of the same region.

24 There is further provided, in accordance with a
25 preferred embodiment of the invention, a method of
26 displaying impedance imaging information comprising:

27 displaying a capacitance map of a region; and

28 simultaneously displaying a conductance map of the same
29 region.

30 There is further provided, in accordance with a
31 preferred embodiment of the invention, a method of
32 displaying impedance imaging information comprising:

33 computing maps of a plurality of imaging measures; and
34 simultaneously displaying the measures.

35 There is further provided, in accordance with a
36 preferred embodiment of the invention, a method of

1 displaying impedance information comprising:
2 computing a plurality of maps of at least one imaging
3 measure at a plurality of frequencies; and
4 simultaneously displaying the maps.
5 There is further provided, in accordance with a
6 preferred embodiment of the invention, a method of
7 differentiating a suspected carcinoma from a suspected
8 atypical hyperplasia comprising:
9 comparing a capacitance map of a region to a
10 conductance map of the same region;
11 classifying a deviation from the surroundings as a
12 suspected atypical hyperplasia if at some frequency less
13 than 500 Hz the capacitance value is lower than that of the
14 surroundings and the conductance value is higher than that
15 of the surroundings; and
16 classifying a deviation from the surroundings as a
17 suspected cancer if at some frequency less than 500 Hz both
18 the capacitance value and the conductance value are
19 higher than that of the surroundings.

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BRIEF DESCRIPTION OF THE DRAWINGS

2 The invention will be more fully understood and
3 appreciated from the following detailed description, taken
4 in conjunction with the drawings in which:

5 Fig. 1 is an overall view of an impedance mapping
6 system especially suitable for breast impedance mapping in
7 accordance with a preferred embodiment of the invention;

8 Fig. 2 is a perspective view of an imaging head
9 suitable for breast impedance mapping in accordance with a
10 preferred embodiment of the invention;

11 Figs. 3A and 3B show partially expanded views of two
12 preferred probe head configurations suitable for use in the
13 imaging head of Fig. 2;

14 Fig. 4 is a top view of a portion of a multi-element
15 probe in accordance with a preferred embodiment of the
16 invention;

17 Fig. 5A is a partial, partially expanded cross-
18 sectional side view of the probe of Fig. 4 along lines V-V,
19 suitable for the probe head configuration of Fig. 3B;

20 Fig. 5B is a partially expanded cross-sectional side
21 view of an alternative probe in accordance with a preferred
22 embodiment of the invention;

23 Fig. 5C shows an alternative embodiment of a multi-
24 element probe, in accordance with a preferred embodiment of
25 the invention;

26 Fig. 6A is a perspective view of a hand held probe in
27 accordance with a preferred embodiment of the invention;

28 Fig. 6B shows a partially expanded bottom view of the
29 probe of Fig. 6A, in accordance with a preferred embodiment
30 of the invention;

31 Fig. 7A is a perspective view of a fingertip probe in
32 accordance with a preferred embodiment of the invention;

33 Fig. 7B shows a conformal multi-element probe;

34 Fig. 8 shows an intra-operative probe used determining
35 the position of an abnormality in accordance with a
36 preferred embodiment of the invention;

1 Fig. 9 shows a laparoscopic probe in accordance with a
2 preferred embodiment of the invention;

3 Fig. 10 shows a biopsy needle in accordance with a
4 preferred embodiment of the invention;

5 Fig. 11A illustrates a method of using the biopsy
6 needle of Fig. 10, in accordance with a preferred embodiment
7 of the invention;

8 Fig. 11B illustrates a portion of a display used in
9 conjunction with the method of Fig. 11A;

10 Fig. 11C shows a biopsy guiding system in accordance
11 with a preferred embodiment of the invention;

12 Fig. 11D shows a frontal biopsy guiding system in
13 accordance with a preferred embodiment of the invention;

14 Fig. 11E shows a lateral biopsy guiding system in
15 accordance with a preferred embodiment of the invention;

16 Fig. 12 shows, very schematically, the inter-operative
17 probe of Fig. 8 combined with a video camera use to more
18 effectively correlate an impedance measurement with
19 placement of the probe.

20 Fig. 13 illustrates a laparoscopic probe according to
21 the invention used in conjunction with a fiber-optic
22 illuminator-imager;

23 Fig. 14 illustrates a display, according to a preferred
24 embodiment of the invention showing both capacitive and
25 conductance images illustrative of atypical hyperplasia;

26 Fig. 15 illustrates a display, according to a preferred
27 embodiment of the invention showing both capacitive and
28 conductance images illustrative of a carcinoma; and

29 Fig. 16 illustrates a method useful for verifying a
30 detected local impedance deviation as being non-artifactual
31 and for estimating the deviation;

32 Figs. 17A and 17B are a block diagram of circuitry
33 suitable for impedance mapping in accordance with a
34 preferred embodiment of the invention.

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1 DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

2 Reference is made to Figs. 1 and 2 which illustrate an
3 impedance mapping device 10 suitable for mapping the
4 impedance of a breast.

5 Mapping device 10 includes an imaging head 12, which is
6 described below, which holds the breast and provides contact
7 therewith for providing electrical excitation signals
8 thereto and for receiving resultant electrical signals
9 therefrom. Signals to and from the head are generated and
10 received by a computer/controller 14 which produces
11 impedance maps of the breast under test for display on a
12 monitor 16. The impedance maps may be stored in
13 computer/controller 14 for later viewing or processing or
14 hard copies may be provided by a hard copy device 18 which
15 may be a laser printer, video printer, Polaroid or film
16 imager or multi-imager.

17 The entire mapping device 10 may be conveniently
18 mounted on a dolly 20 to facilitate placement of the imaging
19 head with respect to the patient.

20 Fig. 1 also shows a hand held probe 100, described in
21 more detail below, and a reference probe 13.

22 Fig. 2 shows imaging head 12 in more detail. Head 12
23 comprises a movable lower plate probe 22 and a stationary
24 upper plate probe 24 which is mounted on a pair of rails 26
25 to allow the distance between plate probes 22 and 24 to be
26 varied.

27 Movement of plate probe 22 along rails 26 may be
28 achieved either by a motor (not shown) including suitable
29 protection against over-pressure as is traditional in X-ray
30 breast imaging, or by hand.

31 Either or both of plate probes 22 and 24 are provided
32 with multi-element probes 28 and 30 respectively, which are
33 described more fully below, which electrically contact the
34 breast with a plurality of sensing elements to optionally
35 provide electrical excitation to the breast and to measure
36 signals generated in response to the provided signals.

1 Alternatively, electrical excitation to the breast is
2 provided by reference probe 13 which is placed on the arm,
3 shoulder or back of the patient, or other portion of the
4 patient.

5 In practice, a breast is inserted between probes 28 and
6 30 and plate probe 24 is lowered to compress the breast
7 between the probes. This compression reduces the distance
8 between the probes and provides better contact between the
9 sensing elements and the skin of the breast. Although
10 compression of the breast is desirable, the degree of
11 compression required for impedance imaging is much lower
12 than for X-Ray mammography, and the mapping technique of the
13 present invention is typically not painful.

14 Alternatively or additionally, the probes are curved to
15 conform with the surface of the breast.

16 Head 12 is provided with a pivot (not shown) to allow
17 for arbitrary rotation of the head about one or more of its
18 axes. This allows for both medio-lateral and crano-caudal
19 maps of the breast to be acquired, at any angular
20 orientation about the breast. Preferably, head 12 may be
21 tilted so that the surfaces of plate probes 22 and 24 are
22 oriented with a substantial vertical component so that
23 gravity assists the entry of the breast into the space
24 between the maximum extent and to keep it from inadvertently
25 falling out. This is especially useful when the patient
26 leans over the plates so that her breasts are positioned
27 downwardly between the plate probes.

28 Furthermore, in a preferred embodiment of the
29 invention, one or both of probes 28 and 30 may be rotated
30 about an axis at one end thereof, by a rotation mechanism 27
31 on their associated plate probes 22 or 24, such as is shown
32 in Fig. 2 for probe 28. Additionally or alternatively,
33 probes 28 and/or 30 may be slidable, as for example along
34 members 31.

35 Such additional sliding and rotating flexibility is
36 useful for providing more intimate skin contact of the

1 probes with the breast, which has a generally conical shape.
2 Furthermore, such flexibility allows for better imaging of
3 the areas of the breast near the chest wall or the rib cage,
4 which are extremely difficult to image in x-ray mammography.

5 Figs. 3A and 3B show partially expanded views of two
6 probe head configurations suitable for use in the imaging
7 head of Fig. 2, in accordance with preferred embodiments of
8 the invention.

9 In the embodiment of Fig. 3A, a preferably removable
10 multi-element probe 62, which is described below in more
11 detail, is attached to a probe head base 50 via a pair of
12 mating multi-pin connectors 51 and 52. A cable 53 couples
13 connector 52 to computer 14. When multi-element probe 62 is
14 inserted into base 50 (that is to say, when connector 51 is
15 fully inserted into connector 52), the relatively stiff
16 bottom of probe 62 rests on ledges 54 formed in the base,
17 such that the surface 55 of the base and the surface of
18 element 62 are preferably substantially coplanar.

19 In the embodiment of Fig. 3B, a series of contacts 82
20 are formed on base 50 and a disposable multi-element probe
21 62' is attached to the contacts as described below with
22 reference to Fig. 5A and 5B. Cable 53 couples the contacts
23 to computer 14.

24 Figs. 4, 5A and 5B show top and side views of a portion
25 of multi-element probe 62' and contacts 74, while Figs. 5A
26 and 5B show a partially expanded cross-sectional side view
27 of probe 62' along lines V-V. While the embodiment shown in
28 Figs. 4, 5A and 5B is especially suitable for the probe head
29 configuration of Fig. 3B, much of the structure shown in
30 these figures 5 is common to multi-element probes used in
31 other configurations described herein.

32 As shown in Figs. 4, 5A and 5B, disposable multi-
33 element probe 62' preferably incorporates a plurality of
34 sensing elements 64, separated by separator or divider
35 elements 66.

36 As shown more clearly in Figs. 5A and 5B, sensing

1 elements 64, comprise a bio-compatible conductive material
2 (for example Neptrode E0751 or Neptrode E0962 Hydrogel
3 distributed by Cambrex Hydrogels, Harriman, NY) such as is
4 sometimes used for ECG probes in a well 70 formed by a
5 first, front, side of a mylar or other flexible, non-
6 conducting substrate 68, such as a thin mylar sheet and the
7 divider elements 66. A suitable thickness for the mylar
8 sheet is approximately 0.2 mm for probe 62'. The substrate
9 is preferably pierced in the center of each well. The hole
10 resulting from the piercing is filled with a conducting
11 material which is also present on the bottom of well 70 and
12 on a second, back, side of substrate 68 to form a pair of
13 electrical contacts 72 and 74 on either side of the
14 substrate and an electrically conducting feed-through 76
15 between the pair of contacts. As shown, a separate contact
16 pair and feed-through is provided for each sensing element.

17 Alternatively, the substrate may be formed of any
18 suitable inert material including plastics such as
19 polyethylene, polypropylene, PVC, etc.

20 Wells 70 may be formed in a number of ways. One method
21 of forming the wells is to punch an array of square holes in
22 a sheet of plastic, such as polypropylene, which is about
23 0.2-1mm thick. This results in a sheet containing only the
24 divider elements. This sheet is bonded to substrate 68 which
25 has been pre-pierced and in which the contacts and feed-
26 throughs have been formed. Another method of forming the
27 wells is to emboss a substrate containing the contacts and
28 feed-throughs to form divider elements in the form of ridges
29 which protrude from the substrate as shown in Fig. 5B. Yet
30 another method of producing the wells is by printing the
31 well walls using latex based ink or other bio-compatible
32 material having a suitable firmness and flexibility. Another
33 method of production is by injection molding of the
34 substrate together with the divider elements. And yet
35 another method of producing the wells is by laminating to
36 the substrate a preformed grid made by die cutting the array

1 of divider elements in a sheet of plastic, injection
2 molding, or other means.

3 The conductors and feed-throughs may be of any
4 conductive material which will provide reliable feed-through
5 plating of the holes. One method of manufacturing the
6 contacts and holes is by screen printing of the contacts on
7 both sides of the substrate. If conductive paste having a
8 suitable viscosity is used, the paste will fill the hole and
9 form a reliable contact between contacts 72 and 74. Although
10 many conductive materials can be used, non-polarizing
11 conductors, such as silver/silver chloride are preferred. A
12 conductive paste suitable for silk screening the conductors
13 onto the substrate is Pad Printable Electrically conductive
14 Ink No. 113-37 manufactured and sold by Creative Materials
15 Inc., Tyngsboro, MA.

16 In general contacts 72 and 74 are only 10-200 microns
17 thick and wells 70 are generally filled with conductive
18 viscous gel material or hydrogel material to within about
19 0.2 mm of the top of the dividing elements. In general, if
20 low separators are used, the hydrogel may be omitted.
21 However, in the preferred embodiment of the invention, the
22 wells are at least partially filled by hydrogel or a similar
23 material.

24 Hydrogel is available in both UV cured and heat cured
25 compositions. In either case a measured amount of uncured
26 semi-liquid hydrogel is introduced into each well and the
27 hydrogel is cured. Alternatively, the wells are filled with
28 the uncured material and a squeegee which is pressed against
29 the top of the divider elements with a predetermined force
30 is moved across the top of the divider elements. This will
31 result in the desired gap between the top of the hydrogel
32 and the top of the wells.

33 In an alternative embodiment of the invention, the
34 hydrogel material is replaced by a sponge material or
35 similar supportive matrix impregnated with conductive
36 viscous gel or the well is simply filled with the conductive

1 gel to the desired height.

2 During use of the probe, the probe is urged against the
3 skin which is forced into the wells and contacts the
4 hydrogel or alternative conductive material. Optionally, a
5 somewhat viscous conductive gel, such as Lectron II
6 Conductivity Gel (Pharmaceutical Innovations, Inc. Newark,
7 NJ), may be used to improve contact with the skin. In this
8 case, the dividing elements will reduce the conduction
9 between the cells such that the substantial independence of
10 the individual measurements is maintained. Alternatively,
11 the conductive gel may be packaged together with the probe,
12 with the conductive gel filling the space between the top of
13 the hydrogel and the top of the wells. The use of a
14 conductive gel is preferred since this allows for sliding
15 movement of the probe and its easy positioning while it is
16 urged against the skin. The separators substantially prevent
17 the conductive gel from creating a low conductance path
18 between adjoining sensing elements and also keep the
19 hydrogel elements from touching each other when the probe is
20 applied to the skin with some pressure.

21 In a further preferred embodiment of the invention, the
22 sensing elements are formed of a conductive foam or sponge
23 material such as silicone rubber or other conductive rubber
24 or other elastomer impregnated with silver or other
25 conductive material, as shown in Fig. 5C. Fig. 5C shows the
26 sensing elements without walls 66. Elements which protrude
27 from the substrate as shown in Fig. 5C may achieve
28 substantial electrical isolation from one another by spacing
29 them far enough apart so that do not contact each other in
30 use or by coating their lateral surfaces with insulating
31 material such as polyethylene or other soft non-conductive
32 plastic or rubber.

33 For relatively short rigid or compressible elements, it
34 has been found that reducing the size of the sensing
35 elements such that no more than 70% (and preferably no more
36 than 50%) of the area of the array is covered is sufficient

1 to reduce the "cross-talk" between adjoining elements to an
2 acceptable level.

3 If sufficiently good isolation is achieved between
4 probe elements by their spacing alone, then foam or other
5 elements without hydrogel and without walls 66 may be
6 provided. Sensing elements such as those shown in Fig. 5C
7 conform and mate to uneven surfaces when pressed against
8 tissue.

9 Multi-element probe 62', which is preferably used for
10 only one patient and then discarded, is preferably removably
11 attached to a probe holder which preferably comprises a
12 printed circuit board 80 having a plurality of contacts 82
13 corresponding to the contacts 74 on the back of the
14 substrate, each PC board contact 82 being electrically
15 connected to a corresponding contact 74 on the substrate.
16 To facilitate alignment of the matching contacts, an
17 alignment guide 90 is preferably provided on or adjacent to
18 PC board 80 (Fig. 4). This guide may consist of a series of
19 guide marks or may consist of a raised edge forming a well
20 into or onto which the substrate is inserted. Conductors
21 within PC board 80 connect each of the contacts to one of
22 the pins of connector 51, which is preferably mounted on PC
23 board 80.

24 Alternatively and preferably, as described below with
25 respect to Fig. 6B, the guide may consist of two or more
26 pins located on or near PC board 80, which fit into matching
27 holes in probe 62'.

28 Alternatively as shown in Fig. 5B, the back side of the
29 embossing of substrate 68 is used as the guide for one or
30 more protruding elements 83 which are preferably mounted on
31 PC board 80. Preferably a plurality of protruding elements
32 are provided to give good alignment of the substrate with
33 the PC board. The elements may run along the periphery of
34 the probe and form a frame-like structure as shown in Fig.
35 5B or may run between the elements or may take the form of x
36 shaped protuberances which match the shape of the embossing

1 at the corners of the wells.

2 Protruding elements 83 may be formed of polycarbonate,
3 acetate, PVC or other common inert plastic, or of a
4 noncorrosive metal such as stainless steel.

5 A wire 84 is connected to each PC contact 82 and is
6 also connected to apparatus which provides voltages to
7 and/or measures voltages and/or impedances at the individual
8 sensing elements 64, as described below.

9 In a preferred embodiment of the invention, conductive
10 adhesive spots 86 preferably printed onto the back of the
11 substrate are used to electrically and mechanically connect
12 contacts 74 with their respective contacts 82. Preferably a
13 conductive adhesive such as Pressure Sensitive Conductive
14 Adhesive Model 102-32 (Creative Materials Inc.) is used.
15 Alternatively, the adhesive used for printing the
16 contacts/feed-throughs is a conducting adhesive and adhesive
17 spots 86 may be omitted. Alternatively, pins, which protrude
18 from the surface of PC board 80 and are connected to wires
19 84 pierce the substrate (which may be pre-bored) and contact
20 the gel or hydrogel in the wells. A pin extending from the
21 substrate may also be inserted into a matching socket in the
22 PC board to form the electrical connection between the
23 sensing element and the PC board. Alternatively, the entire
24 back side of the substrate can be adhered to the printed
25 circuit board surface using an anisotropically conductive
26 thin film adhesive which has a high conductivity between
27 contacts 74 and 82 and which has a low conductivity
28 resulting in preferably many times higher resistance between
29 adjoining contacts than between matching contacts, in
30 practice at least one hundred times different. An example of
31 such adhesive is tape NO. 3707 by MMM Corporation,
32 Minneapolis MN. However, due to the difficulty of applying
33 such material without trapped air bubbles, it may be
34 preferably to apply adhesive only to the contacts
35 themselves. In practice a release liner of polyethylene,
36 mylar or paper with a non-stick surface on one side is

1 provided on the lower side of the adhesive sheet. This liner
2 protects the adhesive layer prior to connection of the
3 disposable multi-element probe to the probe holder and is
4 removed prior to the connection of the probe to the holder.

5 Preferably, the impedance between contacts 82 and skin
6 side of the conducting material in the wells should be less
7 than 100 ohms at 1 kHz and less than 400 ohms at 10 Hz.

8 Impedance between any pair of contacts 82, with the
9 multi-element probe mounted should preferably be greater
10 than 10 kohm at 1 kHz or 100 kohm at 10 Hz.

11 Another suitable material for producing substrates is
12 TYVEK (DuPont) substrate which is made from a tough woven
13 polyolefin material available in various thicknesses and
14 porosities. If such material having a suitable porosity is
15 used, contacts 72 and 74 and feed-through 76 can be formed
16 by a single printing operation with conductive ink on one
17 side of the TYVEK sheet. Due to the porosity of the TYVEK,
18 the ink will penetrate to the other side of the TYVEK and
19 form both contacts and feed-through in one operation.

20 For probe 62 in the embodiment of Fig. 3A, substrate
21 68 is replaced by a relatively rigid PC board which includes
22 conducting wires to attach each of electrical contacts 72 to
23 one of the pins of connector 51 (Fig. 3A) and the rest of
24 the connecting structure of Fig. 5A may be omitted. It
25 should be noted that the choice of using the structure of
26 Figs. 3A or 3B (i.e., probes 62 or 62') is an economic one
27 depending on the cost of manufacture of the probes. While
28 probe 62 is structurally simpler, the disposable portion of
29 probe 62' is believed to be less expensive to manufacture in
30 large quantities. Since it is envisioned that the probes
31 will be used in large quantities and will preferably not be
32 reused, one or the other may be preferable.

33 The other side of the probe is also protected by a
34 cover plate 88 (Figs. 5A and 5B) which is attached using any
35 bio-compatable adhesive to the outer edges of dividers 66
36 (Fig. 5A) and/or to the hydrogel, which is preferably

1 moderately tacky. In one preferred embodiment of the
2 invention, the inner surface of the cover plate 88 is
3 provided with an electrically conductive layer so that the
4 impedance of each sensing element from the outer surface of
5 the hydrogel (or conductive gel) to contact 82, can be
6 measured using an external source. In addition, if a known
7 impedance is connected between the conductive layer and a
8 reference point or a source of voltage, the sensing elements
9 can be tested in a measurement mode similar to that in which
10 they will finally be used.

11 Alternatively, a film RC circuit or circuits may be
12 printed on the inner surface of plate 88 to simulate an
13 actual impedance imaging situation. Alternatively, plate 88
14 may be provided with contacts at each sensing location, and
15 circuitry which may simulate a plurality of actual impedance
16 imaging situations. Such circuitry may include external or
17 integral logic such as programmable logic arrays and may be
18 configurable using an external computer interface. The
19 simulation may provide a distinct RC circuit for each
20 sensing element or may provide a sequence of different
21 circuits to each sensing element to simulate the actual
22 range of measurements to be performed using the probe.

23 Fig. 5B shows a preferred embodiment of cover sheet 88
24 (indicated on the drawing as 88') and its mode of attachment
25 to both the multi-element sensor and the PC board. In this
26 embodiment a multi-element probe 62" is optionally further
27 attached to PC board 80 by an adhesive frame 210 which may
28 be conductive or non-conductive, and which assists in
29 preventing entry of water or gel under sensor 62". Sensor
30 62" is preferably further aligned to PC board 80 by one or
31 more holes 222 with one or more pins 204, which are
32 permanently attached to PC board 80 or to a surface adjacent
33 to PC board 80. While pin 204 is shown as being round, using
34 rectangular, triangular, hexagonal pyramidal or other
35 shapes provides additional alignment of the sensor. In
36 general the upper portion of the pin should be curved for

1 improved electrical contact as described below.

2 The upper exposed surface of pin 204 is conductive,
3 preferably curved and is preferably connected to a signal
4 reference source by a conductor 202 in PC board 80. Cover
5 sheet 88' is made of a single integral sheet of easily
6 deformable polyethylene, Mylar or other suitable plastic.
7 Cover sheet 88' is preferably removably attached to the
8 upper side of multi-element probe 62" by a continuous frame
9 of adhesive 225, which need not be conductive, but which
10 seals around a lip where cover 88' contacts probe 62" to
11 protect the quality and sterility of array 230 and to
12 maintain the moisture content of any medium filling wells
13 70. Cover 88' is coated on the side facing probe 62" with a
14 conductive layer 231, such as any of the various metallic
15 coatings, for example, aluminum or the thin film coating
16 described above.

17 Cover 88' is preferably formed after conductive
18 coating, by embossing, vacuforming or other means, to have
19 depressions 233 in the cover located over corresponding
20 wells 70. The depressions are approximately centered on the
21 center of the wells and held a small distance "61" above
22 the surface of the hydrogel or gel, by means of relatively
23 high sidewalls 226 which are formed at the same time as
24 depressions 233. Furthermore, the surface of cover 88'
25 preferably has a concave shape to match the rounded
26 conductive contact surface of pin 204, from which it is
27 held at a distance "62". Distances 61 and 62 are selected to
28 minimize unintended physical contact between the conductive
29 inner surface of the cover, the contacts in the wells and
30 pin 204, for example, during storage and handling prior to
31 use, which might cause corrosion over time due to
32 electrochemical processes.

33 Distances 61 and 62 are also preferably selected so
34 that application of a nominal force (preferably about one
35 kilogram) against a flat outer surface 232 of cover 88',
36 such as by a weighted flat plate, will establish contact

1 between the inner coating 231 and the upper surface of pin
2 204 and with the sensing elements or the gel in the wells.

3 By establishing this contact, the conductive inner
4 surface 231 is connected, on the one hand to signals source
5 contact 202 and with each sensing element. If the coating is
6 a conductor, the sensing elements are all excited by the
7 signal on line 202; if it is a thin film circuit, the
8 contact is via the thin film circuit. In either event, if
9 line 202 is excited by a signal, the signal will be
10 transmitted to each of the sensing elements, either
11 directly, or via a known impedance.

12 In either case, the multi-element array can be tested
13 by the system and any residual impedance noted and corrected
14 when the probe is used for imaging. If the residual
15 impedance of a given sensing element is out of a
16 predetermined specification, or is too large to be
17 compensated for, the multi-element probe will be rejected.
18 Furthermore, the computer may be so configured that imaging
19 may only take place after determination of the contact
20 impedance of the sensing elements or at least of
21 verification that the probe impedances are within a
22 predetermined specification.

23 While pin 204 is shown as being higher than the top of
24 the wells, the pin may be at the same height as the wells,
25 or even below the wells with the cover being shaped to
26 provide a suitable distance "δ2" as described above.

27 In an alternative embodiment of the invention, the
28 contact surface corresponding to pin 204 is printed on or
29 attached to the surface holding the sensing elements, with
30 contact to the PC board being via a through contact in
31 substrate 68, as for the sensing elements.

32 In yet another embodiment of the invention, the
33 conductive contact surface associated with pin 204 is on the
34 surface holding the sensing elements adjacent to pin 204.
35 Pin 204 supports this surface and contacts the contact
36 surface via one, or preferably a plurality of through

1 contacts. Pin 204 is designed to match the contour of the
2 contact surface and preferably, by such matching, to provide
3 additional alignment of the probe on the PC board.

4 To avoid drying out of the Gel or other potential
5 hazards of limited shelf life, the quality of any of the
6 aforementioned versions of the disposable electrode arrays
7 can be assured by incorporating an identification code,
8 preferably including manufacturer and serial number
9 information and date of manufacture. In a preferred
10 embodiment, the information is coded in a bar code printed
11 on each disposable probe, which is packaged together with at
12 least one other such probe (typically 5-50 probes) in the
13 same packet, which also has the same bar code. A bar code
14 reader, interfaced with the system computer, reads the
15 manufacturing information on the packet and each probe,
16 checking for date and compliance and permitting recording
17 only for a number of patients equal to the number of probes
18 in the packet.

19 In a preferred embodiment of the invention a bar code
20 may be placed on the individual disposable electrode arrays
21 which can be read by a bar code reader installed in or under
22 the PC board, for example near reference numeral 83 of Fig.
23 5B.

24 While the invention has been described in conjunction
25 with the preferred embodiment thereof, namely a generally
26 flat, somewhat flexible structure, suitable for general use
27 and for breast screening, other shapes, such as concave
28 structures (e.g., brassiere cups) or the like may be
29 preferable, and in general the shape and configuration of
30 the detectors will depend on the actual area of the body to
31 be measured. For example cylindrical arrays can be useful in
32 certain situations, for example in intra-rectal examinations
33 of the prostate or colon or inside vessels. In this context,
34 a probe according to the invention is also useful for
35 measurements inside the body, for example gynecological
36 measurements or measurements in the mouth, where the probe

1 is inserted into a body cavity and contacts the lining of
2 the cavity, and probes having shapes which correspond either
3 flexibly or rigidly to the surface being measured can be
4 used. For example, a multi-element probe in accordance with
5 the invention may be incorporated into or attached to a
6 laparoscopic or endoscopic probe.

7 Furthermore, sterilized probes can be used in invasive
8 procedures in which the probe is placed against tissue
9 exposed by incision. In this context, the term "skin" or
10 "tissue surface" as used herein includes such cavity lining
11 or exposed tissue surface.

12 In a preferred embodiment of the invention, PC board 80
13 and as many elements as possible of probe 62' (or the board
14 of probe 62) are made of transparent or translucent
15 material, so as to provide at least some visibility of the
16 underlying tissue during placement of probe 62. Those
17 elements of the probe and conductors in the PC board, to the
18 extent that they are opaque should be made as small as
19 practical to provide the largest possible view to a
20 technician or clinician to aid in placement of the probe.
21 Furthermore, probe 62 is slidably displaceable when used
22 with the above-mentioned conductive gel to permit moderate
23 lateral adjustment of the probe position, to aid in
24 placement, to ensure good contact between each element and
25 the tissue surface to be measured, and to enable the user to
26 rapidly verify whether detected abnormalities are artifacts
27 due to poor contact or are genuine objects, since artifacts
28 remain stationary or disappear entirely when the probe is
29 moved while genuine objects just move in a direction
30 opposite to the direction of movement of the probe.

31 The general shape and size of the multi-element probe
32 and the size of the conductive sensing elements will depend
33 on the size of the area to be measured and on the desired
34 resolution of the measurement. Probe matrix sizes of greater
35 than 64 x 64 elements are envisioned for viewing large areas
36 and probes which are as small as 2 x 8 elements can be

1 useful for measuring small areas. Element size is preferably
2 between 2 mm square and 8 mm square; however, larger sizes
3 and especially smaller sizes can be useful under certain
4 circumstances. For the breast probe 62 described above, 24 x
5 32 to 32 x 40 elements appear to be preferred matrix sizes.

6 Fig. 6A shows a perspective view of a hand held probe
7 100 in accordance with a preferred embodiment of the
8 invention. Probe 100 preferably comprises two probe heads, a
9 larger head 102 and a zoom sensor head 104. A handle 106
10 connects the sensor heads, houses switching electronics and
11 provides means for holding and positioning the probes.
12 Handle 106 also optionally incorporates a digital pointing
13 device 105 such as a trackball, pressure sensitive button or
14 other such joystick device. Incorporation of a pointing
15 device on the probe enables the operator to control the
16 system and input positional information while keeping both
17 hands on either the probe or patient. As described below,
18 the digital pointing device can be used to indicate the
19 position on the patient's body at which the image is taken.

20 Fig. 6B shows a partially expanded bottom view of probe
21 100 of Fig. 6A, in accordance with a preferred embodiment of
22 the invention. Where applicable, like parts of the probes
23 throughout this disclosure are similarly numbered. Starting
24 from the bottom of Fig. 6B, the top half of a housing 108A
25 has a well 110 formed therein. A clear plastic window 112 is
26 attached to the edge of well 110, and a printed circuit on a
27 relatively transparent substrate, such as Kapton, designated
28 by reference 80' (to show its similarity to the
29 corresponding unprimed element of Fig. 5) is placed on
30 window 112. A flexible print cable 114 connects the contacts
31 on printed circuit 62' to acquisition electronics 116. A
32 cable 118 connects the acquisition electronics to the
33 computer. A second similarly constructed, but much smaller
34 zoom sensor probe head is attached to the other end of probe
35 100. Either of the larger or smaller heads may be used for
36 imaging.

1 A lower half of housing 108B, encloses electronics 116
2 and print 80', whose face containing a series of contacts
3 82', is available through an opening 120 formed in the lower
4 housing half 108B. A mounting frame 122 having two alignment
5 pins 124 holds print 80' in place. Mounting and connecting
6 screws or other means have been omitted for simplification.

7 A disposable multi-element probe 62', similar to that
8 of Fig. 5 is preferably mounted on the mounting frame to
9 complete the probe.

10 Fig. 7A is a perspective view of a fingertip probe 130
11 in accordance with a preferred embodiment of the invention
12 as mounted on the finger 132 of a user. Probe 130 may be
13 separate from or an integral part of a disposable glove,
14 such as those normally used for internal examinations or
15 external palpation. The fingertip probe is especially useful
16 for localizing malignant tumors or investigating palpable
17 masses during surgery or during internal examinations. For
18 example, during removal of a tumor, it is sometimes
19 difficult to determine the exact location or extent of a
20 tumor. With the local impedance map provided by the
21 fingertip probe 130 and the simultaneous tactile information
22 about the issue contacted by the probe, the tumor can be
23 located and its extent determined during surgery. In a like
24 fashion, palpable lumps detected during physical breast (or
25 other) examination can be routinely checked for impedance
26 abnormality.

27 Fig. 7B shows a flexible probe array 140 which is shown
28 as conforming to a breast being imaged. Probe array 140
29 comprises a plurality of sensing elements 141 which contact
30 the tissue surface which are formed on a flexible substrate.
31 Also formed on the flexible substrate are a plurality of
32 printed conductors 142 which electrically connect the
33 individual sensing elements 141 to conductive pads on the
34 edge of the substrate. A cable connector 144 and cable 145
35 provide the final connection link from the sensing elements
36 to a measurement apparatus. Alternatively, the flexible

1 array may take a concave or convex shape such as a cup
2 (similar in shape to a bra cup) which fits over and contacts
3 the breast.

4 The flexible substrate is made of any thin inert
5 flexible plastic or rubber, such as those mentioned above
6 with respect to Fig. 5A. Array 140 is sufficiently pliant
7 that, with the assistance of viscous gel or conductive
8 adhesive, the sensor pads are held in intimate contact with
9 the skin or other surface, conforming to its shape.

10 Fig. 8 shows an intra-operative paddle type probe 140
11 used, in a similar manner as probe 130, for determining the
12 position of an abnormality in accordance with a preferred
13 embodiment of the invention. This probe generally includes
14 an integral sensing array 143 on one side of the paddle.
15 Preferably, the paddle is made of substantially transparent
16 material so that the physical position of the array may be
17 determined and compared with the impedance map.

18 Fig. 9 shows a laparoscopic probe 150 in accordance
19 with a preferred embodiment of the invention. Probe 150 may
20 have a disposable sensing array 152 mounted on its side or
21 the sensing array may be integral with probe 150, which is
22 disposable or sterilizable.

23 Multi-element probes, such as those shown in Figs. 7, 8
24 and 9, are preferably disposable or sterilizable as they are
25 generally used inside the patients body in the presence
26 of body fluids. In such situations, there is generally no
27 need or desire for a conductive gel in addition to the
28 probes themselves. Generally, printed sensing elements, such
29 as those printed with silver-silver chloride ink, or sensing
30 elements formed of conductive silicone, hydrogel or of a
31 conductive sponge may be used. While in general it is
32 desirable that the sensing elements on these multi-element
33 probes be separated by physical separators 66 (as shown in
34 Fig. 5), under some circumstances the physical distance
35 between the elements is sufficient and the separators may be
36 omitted.

1 When performing a needle biopsy, a physician generally
2 relies on a number of indicators to guide the needle to the
3 suspect region of the body. These may include tactile feel,
4 X-Ray or ultrasound studies or other external indicators.
5 While such indicators generally give a reasonable
6 probability that the needle will, in fact take a sample from
7 the correct place in the body, many clinicians do not rely
8 on needle biopsies because they may miss the tumor.

9 Fig. 10 shows a biopsy needle 154, in accordance with a
10 preferred embodiment of the invention, which is used to
11 improve the accuracy of placement of the needle. Biopsy
12 needle 154 includes a series of sensing elements 156 spaced
13 along the length of the probe. Leads (not shown) from each
14 of these elements bring signals from the elements to a
15 detection and computing system such as that described below.
16 Elements 156 may be continuous around the circumference, in
17 which case they indicate which portion of the needle is
18 within the tumor to be biopsied. Alternatively,
19 the electrodes may be circumferentially segmented (a lead
20 being provided for each segment) so that information as to
21 the direction of the tumor from the needle may be derived
22 when the needle is not within the tumor. Such an impedance
23 sensing biopsy needle can be used, under guidance by
24 palpation, ultrasound, x-ray mammography or other image from
25 other image modalities (preferably including impedance
26 imaging as described herein), taken during the biopsy or
27 prior to the biopsy to improve the accuracy of placement of
28 the needle. In particular, the impedance image from the
29 needle may be combined with the other images in a display.
30 While this aspect of the invention has been described using
31 a biopsy needle, this aspect of the invention is also
32 applicable to positioning of any elongate object such as an
33 other needle (such as a localizing needle), an endoscopic
34 probe or a catheter.

35 Returning now to Figs. 1-3 and referring additionally
36 to Figs. 11-14, a number of applications of multi-element

1 probes are shown. It should be understood that, while some
2 of these applications may require probes in accordance with
3 the invention, others of the applications may also be
4 performed using other types of impedance probes.

5 Fig. 11A shows the use of the biopsy needle in Fig. 10
6 together with an optional ultrasound imaging head in
7 performing a biopsy. A breast 160 having a suspected cyst or
8 tumor 162 is to be biopsied by needle 154. An ultrasound
9 head 164 images the breast and the ultrasound image, after
10 processing by an ultrasound processor 166 of standard design
11 is shown on a video display 168. Of course, the ultrasound
12 image will show the biopsy needle. The impedance readings
13 from probe 154 are processed by an impedance processor 170
14 and are overlaid on the ultrasound image of the biopsy
15 needle in the display by a video display processor 172.

16 In one display mode, the portions, as shown in Fig. 11B
17 of the needle which are within the tumor or cyst and which
18 measure a different impedance from those outside the tumor,
19 will be shown in a distinctive color to indicate the portion
20 of the needle within the tumor or cyst. In a second display
21 mode, the impedance measured will be indicated by a range of
22 colors. In yet a third embodiment of the invention, in which
23 circumferentially segmented sensing elements are employed,
24 the impedance processor will calculate radial direction of
25 the tumor from the needle and will display this information,
26 for example, in the form of an arrow on the display.

27 The image sensing biopsy needle can also be used with
28 one or more imaging arrays (28, 30) such as those shown in
29 Fig. 6 or Fig. 3B to impedance image the region to be
30 biopsied during the biopsy procedure. Alternatively, at
31 least one of the arrays can be an imaging array of the non-
32 impedance type. In one preferred embodiment, shown in Fig.
33 11C, the needle is inserted through an aperture (or one of a
34 plurality of apertures) 174 in a multi-element probe which
35 is imaging the region. The region may, optionally, be
36 simultaneously viewed from a different angle (for example at

1 90° from the probe with the aperture) with an other
2 impedance imaging probe. In the case that both arrays 28 and
3 30 are impedance imaging arrays, the biopsy needle or other
4 elongate object can either have impedance sensing or not,
5 and the two images help direct it to the region. The probe
6 with one or more apertures is sterile and preferably
7 disposable. This biopsy method is shown, very schematically,
8 in Fig. 11C.

9 In an alternative preferred embodiment of the
10 invention, only the perforated plate through which the
11 needle or elongate object is passed is an imaging array. In
12 this case the array through which the needle passes give a
13 two dimensional placement of the impedance abnormality while
14 an imaging or non-imaging impedance sensor on the needle
15 gives an indication of when the needle has reached the
16 region of impedance abnormality, as described above.

17 Alternative guiding systems for frontal and lateral
18 breast biopsy or for guiding an elongate element to a
19 desired impedance region of the body are shown in Figs. 11D
20 and 11E, respectively.

21 Fig. 11D shows a system for in which two relatively
22 large plate multi-element probes 28, 30 are placed on
23 opposite sides of the desired tissue, shown as a breast 160
24 of a prone patient 161. Sensor array probes 28 and 30 are
25 held in position by positional controller 181 via rotatable
26 mounts 191. A mount 198 positions a biopsy needle 199 within
27 the opening between probe arrays 28 and 30, and is operative
28 to adjust its height. A suspicious region 183 which is
29 located at positions 184 and 185 on arrays 28 and 30
30 respectively as described herein, which information is
31 supplied to a CPU 197, which determines the position of the
32 suspicious region for controller 181. The controller then
33 inserts the needle into the suspicious region, for example,
34 to take the biopsy. Biopsy needle 199 is preferably of the
35 type shown in Fig. 10 to further aid in positioning of the
36 needle. As indicated above, this is not required for some

1 embodiments of the invention.

2 Alternatively, biopsy needle 199 may be inserted
3 through holes formed between the elements of probes 28
4 and/or 30 as described above. Furthermore, while automatic
5 insertion of the biopsy needle is shown in Fig. 11D, manual
6 insertion and guidance based on impedance images provided by
7 the probes is also feasible.

8 Fig. 11E shows a system similar to that of Fig. 11D in
9 which the imaging and biopsy needle insertion is from the
10 side of the breast, rather than from the front. Operation of
11 the method is identical to that of Fig. 11D, except that an
12 additional probe 29 may be provided for further localization
13 of suspicious region 183. Alternatively, one or two of the
14 probes may be substituted by plates of inert material for
15 holding and positioning the breast.

16 It should be noted that while the breast has been used
17 for illustrative purposes in Figs. 11A through 11E, the
18 method described is applicable to other areas of the body,
19 with necessary changes due to the particular physiology
20 being imaged.

21 Fig. 12 shows, very schematically, the intra-operative
22 probe of Fig. 8 combined with a video camera 256 to more
23 effectively correlate the impedance measurement with the
24 placement of the probe on the body. An intra-operative probe
25 140 preferably having a number of optically visible
26 fiduciary marks 146 is placed on the suspect lesion or
27 tissue. A video camera 256 sequentially views the area
28 without the probe and the same area with the probe in place
29 and displays a composite image on a video display 258 after
30 processing by a processor 260. Processor 260 receives the
31 impedance data from probe 140, determines the positions of
32 the fiduciary marks from the video image and superimposes
33 the impedance image on the video image, with or without the
34 probe, which is displayed on display 258.

35 Fig. 13 shows a laparoscopic or endoscopic probe 250
36 used in conjunction with a fiber-optic illuminator/imager

1 252. In this embodiment, the laparoscopic impedance probe,
2 which is formed on a flexible, preferably extendible paddle,
3 is viewed by the illuminator/imager which is preferably a
4 video imager, which is well known in the art. Probe 250 can
5 be either round or flat, depending on the region to be
6 imaged. When the imager views a suspicious lesion or tissue,
7 probe 250 is extended to determine the impedance properties
8 of the lesion. The combination of probe 250 and imager 252
9 may be incorporated in a catheter 254 or other invasive
10 element appropriate to the region of the body being
11 investigated.

12 Optically visible fiduciary marks 253 on probe 250 are
13 preferably used to determine the position of probe 250
14 within the video image of the tissue seen by fiber-optic
15 illuminator/imager 252, in a manner similar to that
16 discussed above with respect to Fig. 12.

17 In a preferred embodiment of a system using any of the
18 biopsy needle, intra-operative probe, finger tip probe or
19 other embodiments described above, an audible sound
20 proportional to an impedance parameter measured by the
21 needle or other sensor in or on the body is generated by the
22 system computer. This feature may be useful in situations
23 where the probe is placed in locations which are difficult
24 to access visually, such as suspected lesions during
25 surgery. Such an audible sound could include any kind of
26 sound, such as a tone whose frequency is proportional to the
27 measured parameter or similar use of beeps, clicks, musical
28 notes, simulated voice or the like. This feature can also be
29 used for non-surgical procedures such as rectal, vaginal or
30 oral examinations, or other examinations.

31 Fig. 16 shows methods useful for estimating the depth
32 of a lesion and also for determining if a image contains a
33 true lesion or an artifact.

34 A breast or other region 160 is imaged by a probe 270,
35 for example, the probe of Figs. 1-3 or Figs. 6A and 6B. The
36 depth of a local impedance deviation can be estimated by

1 palpating the breast or other region by a finger 272 or a
2 plunger 274. The displacement of the local deviation on the
3 image will be maximized when the palpation is at the same
4 level as the lesion. It should also be understood that,
5 where palpation causes movement of the local deviation on
6 the impedance image, this is an indication that the
7 deviation is "real" and not an artifact.

8 In a similar manner, application of variable
9 compression to the imaging probe will result in a variation
10 of the distance from the probe to deviation under the probe.
11 This distance variation will cause a corresponding variation
12 in the size and intensity of the deviation, thus helping to
13 verify that the deviation is not artifactual.

14 Alternatively or additionally, the probe can be moved
15 along the surface of the tissue without moving the tissue.
16 In this case, surface effects will have a tendency to either
17 disappear or to move with the probe (remain stationary in
18 the image) while real anomalies will move, on the image, in
19 the opposite direction from the movement of the probe.

20 Alternatively or additionally, the probe and the tissue
21 can be moved together without moving the underlying
22 structure (such as the bones). Tissue lesions will remain
23 relatively stationary in the image while bone artifacts will
24 move in the opposite direction.

25 In operation, a system according to the present
26 invention measures impedance between the individual sensing
27 elements and some reference point (typically the signal
28 source point) at some other place on the body. Generally, in
29 order to produce an interpretable impedance image, the
30 sensing elements in the multi-element probe should detect
31 distortions in the electric field lines due solely to the
32 presence of a local impedance difference between embedded
33 tissue of one type (for example, a tumor) and surrounding
34 tissue of another type (for example, normal adipose tissue).

35 To avoid distortion in the field lines, the reference
36 point is typically placed far from the sensor array, all

1 sensing elements are all at ground or virtual ground, and
2 the current drawn by the elements is measured. Since the
3 probe is at ground (an equipotential) the electric field
4 lines (and the current collected by the elements) are
5 perpendicular to the surface of the multi-element probe. In
6 principle, if there are no variations of impedance below the
7 probe, each element measures the integrated impedance below
8 the element. This first order assumption is used in the
9 determination of the position and/or severity of a tumor,
10 cyst or lesion. It is clear, however, that the multi-element
11 probe covers only a portion of even the organ which is being
12 imaged. The area outside the area of the probe is not at
13 ground potential, causing the field lines to bend out at the
14 periphery of the probe, biasing the edge of the impedance
15 image.

16 To reduce this effect, a conductive "guard ring" is
17 provided around the edge of the imaged area to draw in and
18 straighten the field lines at the edge of the imaged area.
19 This guard ring, if one is desired, can consist of merely
20 ignoring the, presumably distorted, currents drawn by the
21 elements at (or near) the edge of the probe and ignoring the
22 measurements made by these elements.

23 Furthermore, to possibly reduce the baseline impedance
24 contributed to the local impedance image by tissue between
25 the remote signal source and the region near the probe, an
26 additional reference electrode may be placed on the
27 patient's body relatively near the multi-element probe. For
28 example, if the source is placed at the arm of the patient
29 and the breast is imaged from the front, a reference
30 electrode for sensing a reference voltage can be placed at
31 the front of the shoulder of the patient. The measured
32 impedances are then reduced by the impedance value of the
33 reference electrode. Alternatively, the impedance values of
34 the elements of the multi-element probe are averaged to form
35 a reference impedance, and the display of the impedance map
36 is corrected for this reference impedance.

1 One way to substantially avoid at least some of the
2 above- mentioned problems is to use the apparatus shown in
3 Figs. 1-3. As indicated above, the apparatus incorporates
4 two probe heads 28 and 30. The breast to be imaged is placed
5 between the probe heads and the breast is compressed by the
6 heads (although generally to a lesser degree than in X-Ray
7 mammography) so that the breast forms a relatively flat
8 volume and fills the region between the probes. It should be
9 noted that, if the current is measured at each of the
10 sensing elements in both probes, then two somewhat different
11 images of the same region are generated. Avoidance of the
12 problems also results when the two multi-element probes are
13 not parallel as described above.

14 It should be noted that when used on breasts, the
15 images produced by the pair of large, flat probes of Fig. 3
16 have the same geometric configuration as standard
17 mammograms. Furthermore if used in the same compression
18 orientations, the impedance images can be directly compared
19 to the corresponding mammograms. In one preferred embodiment
20 of the invention, mammograms corresponding to the impedance
21 images to be taken are digitized, using film scanning or
22 other digitization means known in the art, and entered into
23 the system computer. If the mammogram is already digital,
24 such as may be provided by a digital mammogram, the image
25 file can be transferred from the mammogram.

26 The mammograms and impedance images can be overlaid or
27 otherwise combined to form a single image. Such an image
28 could highlight those areas of the mammogram in which the
29 impedance is particularly low or high. Such a combined image
30 thus presents two independent readouts (impedance and
31 radiographic density) of the same well defined anatomical
32 region in a known geometric orientation, to facilitate
33 interpretation, correlation with anatomy and localization.

34 It is well known that the resolution of objects in an
35 impedance image is reduced with distance of the object from
36 the probe. Thus, it is possible to estimate the distance of

1 the object from the two probes based on the relative size of
2 the same object on the two different probes. As indicated
3 above, two opposing views of the breast may be taken. This
4 would provide further localization of the object.

5 In one mode, the sensing elements of one probe are all
6 electronically floating while the elements of the other
7 probe are at a virtual ground (inputs to sensing
8 electronics), and a remote signal source is used, as
9 previously described. After an image is obtained from the
10 one probe, the roles of the two probes are reversed to
11 obtain an image from the other probe.

12 Alternatively, if all of the elements of one of the
13 flat probes are electrified to the same voltage and the
14 measuring probe is kept at virtual ground, the currents
15 drawn from and received by the elements of both probes form
16 a two dimensional admittance image of the region between the
17 probes.

18 In a further preferred embodiment of the invention, one
19 or a few closely spaced sensing elements on one of the
20 probes is electrified, and the others are left floating.
21 This would cause a beam-like flow of current from the
22 electrified elements to the other sensing elements on the
23 other probe. The object would disturb this flow causing
24 impedance variations which are strongest for those elements
25 which are in the path of the current disturbed by the
26 object. If a number of such measurements are made with, each
27 with a different group of electrodes being electrified, then
28 good information regarding the position of the object can be
29 obtained.

30 In practice, as indicated above, orthogonal views of
31 the breast are taken giving additional position information.

32 In preferred embodiments of the invention the breast is
33 imaged at a plurality of frequencies and both the real and
34 imaginary parts of the impedance are calculated. The
35 sensitivity of the detection of malignant tissue is a
36 function of frequency, and, for a particular frequency, is a

1 function of the impedance measure or characteristic used for
2 imaging, for example, real part of the impedance (or
3 admittance), imaginary part of the impedance (or
4 admittance), absolute value of the impedance (or
5 admittance), phase of the impedance (or admittance), the
6 capacitance or some function of the impedance or of
7 admittance components.

8 In a practical situation, an impedance measure should
9 give the maximum contrast between a malignancy and non-
10 malignant tissue. It is therefore desirable to determine the
11 frequency or combination of frequencies which give maximum
12 detectability and to determine it quickly. One method of
13 determining the frequency is to perform swept frequency
14 measurements and to use the frequency or combination of
15 frequencies which results in the best contrast.
16 Alternatively, a number of images taken at relatively close
17 frequencies can be used. It is believed that for many
18 purposes, at least four samples should be taken in the range
19 between and including 100 and 400 Hz and, preferably, at
20 least one or two additional images are taken at frequencies
21 up to 1000 Hz.

22 A second method is to use a pulsed excitation and
23 Fourier analysis to determine impedance over a range of
24 frequencies. The optimum frequency or frequencies determined
25 from the swept or pulsed measurement are then used in a
26 single or multiple frequency measurement. A pulse shape
27 which has been found useful in this regard is a bi-polar
28 square pulse having equal positive and negative going pulses
29 of 5-10 millisecond duration and fast rise and fall times.

30 A number of measures of the impedance, as described
31 below, have been found useful for comparing different areas
32 of the image. Generally, it is useful to display a gray
33 scale or pseudo-color representation of the values of the
34 impedance measure, either on a linear scale or where the
35 square of the impedance measure is displayed. Also useful is
36 an "absorption scale" where the value of an impedance

1 measure, v, is displayed as:

2 $d(v) = (\max - 1) * (\exp(v * (\max - 1) - 1)) / (\max - 1)$,

3 where max is the maximum normalized value of v. Generally,
4 the display is most useful when the measure is normalized,
5 either by division or subtraction of the minimum or average
6 value of the measure in the display.

7 Furthermore, the display may be automatically windowed
8 to include only those values of the impedance measure
9 actually in the image, or to include a relative window of
10 selectable size about the average value of the impedance
11 measure. The range of values to be displayed may also be
12 determined using a baseline average value measured at a
13 region remote from irregularities, i.e., remote from
14 the nipple of the breast. Alternatively, the baseline
15 average may be a predetermined average value as measured for
16 a large group of patients. Alternatively, a reference region
17 on the image may be chosen by the user to determine the
18 baseline average to be used for windowing.

19 While the display may show the exact measure for each
20 pixel as is conventional, for example, in displays of
21 nuclear medicine images, in a preferred embodiment of the
22 invention the display is an interpolated image formed by
23 quadratic or cubic spline interpolation of the impedance
24 measure values. This type of display removes the annoying
25 checkerboard effect of the relatively low resolution
26 impedance image without any substantial loss of spatial or
27 contrast detail.

28 The measures of impedance which have been found useful
29 for comparing different areas of the image may be grouped as
30 single frequency measures and polychromatic measures.

31 Single frequency measures include the admittance,
32 capacitance, conductance and phase of the admittance. These
33 measures may be measured at some predetermined frequency, at
34 which the sensitivity is generally high, or at a frequency
35 of high sensitivity determined by a preliminary swept or
36 pulsed measurement.

1 Polychromatic impedance measures are generally based on
2 a spectral curve based on fitting a set of capacitance (C)
3 and conductance (G) values determined at a plurality of
4 frequencies using linear interpolation, quadratic
5 interpolation, cubic spline, band limited Fourier
6 coefficients, or other methods known in the art.

7 One polychromatic measure is a spectral width measure.
8 For a give pixel or region of interest the value of both the
9 G and C parameters fall with frequency. The spectral width
10 is the width of the spectrum (to a given percentage fall in
11 the chosen parameter) as compared to the value at some low
12 frequency, for example 100 Hz. If the parameter does not
13 fall by the given percentage in the measured range it is
14 assigned an impedance measure equal to the full measured
15 bandwidth.

16 A second polychromatic measure is a spectral quotient
17 in which the impedance measure is the ratio of the measured
18 value of G or C parameters at two preset frequencies, which
19 may be user selected, or which may be selected based on the
20 swept or pulsed measurements described above. This measure,
21 as all of the others may be displayed on a per-pixel basis
22 or on the basis of a region of interest of pixels, chosen by
23 the user.

24 A third type of polychromatic measure is based on a
25 Relative Difference Spectrum determination. In this measure,
26 the capacitance or conductance for a given region of
27 interest (or single pixel) is compared to that of a
28 reference region over the spectrum to determine a numerical
29 difference between the two as a function of frequency. The
30 thus derived Relative Difference Spectrum is then analyzed.
31 For example, a spectral width measure as described above has
32 been found to be a useful measure of abnormalities. Normally
33 the width is measured where the relative difference spectrum
34 passes from positive to negative, i.e., where the C or G is
35 equal to that of the reference region.

36 A fourth type of polychromatic measure is based on a

1 Relative Ratio Spectrum determination. This is similar to
2 the Relative Difference Spectrum, except that the ratio of
3 the values between the reference area and the region of
4 interest is used. A spectral width measure can be determined
5 for this spectrum in the same manner as for the Relative
6 difference Spectrum. Normally, the width is measured where
7 the ratio is 1.

8 A fifth polychromatic measure which may be useful is
9 the maximum of one of the other polychromatic measures, for
10 example, the capacitance, conductance, Relative Difference
11 Spectrum, Relative Ratio Spectrum, etc.

12 In impedance measurements of the breast in both men and
13 women, normal breast tissue has a low capacitance and
14 conductivity, except in the nipples, which have a higher C
15 and G values than the surrounding tissue with the maximum
16 obtained at the lowest frequency recorded, typically 100 Hz.
17 The nipple capacitance and conductance remains higher than
18 the surrounding tissue up to about 1400 Hz for fertile
19 patients and up to about 2500 Hz for older patients (which
20 is reduced to 1400 Hz for older patients by estrogen
21 replacement therapy). These frequencies represent the normal
22 range of spectral widths for the Relative and Difference
23 Spectra. Tumors can be recognized by very high C and G
24 relative ratio or relative difference values up to 2500 Hz
25 or even higher.

26 Capacitance and conductance values are measured by
27 comparing the amplitude and phase of the signal received by
28 the sensing elements. Knowing both of these measures at the
29 same points is useful to proper clinical interpretation. For
30 example, as illustrated below in Fig. 14, a region of
31 elevated conductivity and reduced capacitance (especially at
32 relatively low frequencies, most preferably less than 500
33 Hz, by generally below 2500 Hz and also below 10 kHz) is
34 associated with benign, but typically pre-cancerous atypical
35 hyperplasia while, as shown in Fig. 15, cancer typically has
36 both elevated capacitance and conductivity over, generally,

1 a wide frequency range, as compared to the surrounding
2 tissue. Proper differential diagnosis is aided by having the
3 frequency samples be close enough together so that changes
4 in the conductivity and capacitance in the low frequency
5 range can be tracked. This also requires the display of both
6 capacitance and conductance or the use of an impedance
7 measure which is based on an appropriate combination of the
8 two.

9 Methods for calculating C and G are given in the
10 abovementioned US patents 4,291,708 and 4,458,694, the
11 disclosures of which are incorporated herein by reference. A
12 preferred embodiment of the invention takes advantage of the
13 calibration capability inherent in the use of cover plates
14 as shown in Figs. 5A and 5B. It can be shown that if the
15 received waveform is sampled at a fixed spacing, δ , such
16 that N samples are taken in each cycle, then the real and
17 imaginary values of the impedance can be determined as:

18

$$19 \quad G = \Sigma(g_n(V_{(n+\frac{1}{2}N)} - V_n)),$$

20 and

$$21 \quad \omega C = \Sigma(c_n(V_{(n+\frac{1}{2}N)} - V_n)),$$

22 where g_n and c_n are constants determined by a calibration
23 procedure and V_n is the voltage measured at the nth sampling
24 point (out of N). The first sample is taken at zero phase of
25 the reference signal.

26 One relatively easy way to determine the constants is
27 to perform a series of measurements when cover plate is in
28 contact with the sensing elements as described above and a
29 known impedance is placed between the transmitter and the
30 cover plate. Since N coefficients are required for
31 determining g_n and c_n for each frequency, N values of
32 admittance and N measurements are required. For example, if
33 N=4 (four samples per cycle) four different measurements are
34 taken and the sampled signal values are entered into the
35 above equations to give N equations, which are then solved
36 for the values of the coefficients. The higher the number of

1 samples, the greater the accuracy and noise immunity of the
2 system, however, the calibration and computation times are
3 increased.

4 Alternatively, fewer samples are taken and values for a
5 number of measurements are averaged, both in the calibration
6 and clinical measurements to reduce the effects of noise.

7 Artifactual abnormalities in the impedance image can be
8 caused by such factors as poor surface contact or
9 insufficient conductive coupling on some or all of the
10 sensing elements, the presence of air bubbles trapped
11 between probe and tissue and normal anatomical features such
12 as bone or nipple.

13 Bubbles can be recognized by their typically lower C
14 and G values compared to background, often immediately
15 surrounded by pixels with much higher C and G. Bubbles can
16 be verified and eliminated by removing the probe from the
17 skin and repositioning it, and or by applying additional
18 conductive coupling agent. Contact artifacts can be
19 determined and accounted for in real time by translating the
20 probe and viewing the image as described above. Artifacts
21 either disappear or remain fixed with respect to the pixels,
22 while real tissue features move, on the image, in a
23 direction opposite from the motion of the probe.
24 Additionally, as described above, if the tissue beneath the
25 skin is physically moved, while the probe and skeletal
26 structure is kept fixed, only real tissue features will
27 move. If the feature remains static, it is either a skin
28 feature or bone.

29 If as described above, the probe and the tissue are
30 moved together without moving the underlying structure (such
31 as the bones). Tissue lesions and surface effects will
32 remain relatively stationary in the image while bone
33 artifacts will move in the opposite direction, thus
34 distinguishing them from other impedance deviations.

35 Fig. 14 shows one example of a display, according to a
36 preferred embodiment of the invention. In this display,

1 capacitance and conductivity images at two positions on a
2 breast are shown, together with an indication of the
3 positions on the breast at which these images were acquired.

4 In particular, as seen in Fig. 15, the display includes
5 the capability of displaying up to five sets of capacitance
6 and conductance images in the five sets of smaller squares.
7 These images are associated with probe areas indicated as
8 numbers 1-5 on the breast image shown in the display. In
9 practice, the examiner manipulates a joystick or other
10 digital pointing device, such as device 105 shown in Fig.
11 6A. This device is manipulated until a square is
12 appropriately placed on the breast image. The examiner then
13 presses a button which causes a pair of impedance images to
14 be stored and displayed on the screen in an appropriate
15 square, and the indicated position to be displayed on the
16 physiological (breast) drawing. The small images are
17 numbered from left to right. Preferably, the examiner can
18 scale the physiological image so that the dimensions of the
19 breast shown and the extent of the probe array are
20 compatible. It should be understood that during the
21 placement of the probe, real time images (acquired about
22 once every 50-80 msec) of the capacitance and the
23 conductance are shown, for example in the large squares to
24 the left of the display.

25 Fig. 14, which represents an actual imaging situation
26 shows, in the leftmost of the small images, a situation in
27 which a small atypical hyperplasia which was previously
28 detected by other means. This position shows an elevated
29 conductivity and a very slightly reduced capacitance. In
30 position 2, which is also shown in the two large squares to
31 the right of the display, a previously unsuspected area
32 having a capacitance/conductance profile characteristic of
33 atypical hyperplasia is detected.

34 Fig. 15 shows a study typical of multiple suspected
35 sites of carcinoma (in positions 2 and 4). The images of
36 position 4 are shown in enlarged format at the left of the

1 image. In these sites, both the capacitance and conductance
2 are elevated with respect to their surroundings.

3 Alternatively, a composite image such as the image of
4 the sum of the capacitance and conductance images, their
5 product, their sum or their ratio can be displayed to give a
6 similar indication of the type of detected anomaly. A color
7 coded composite image can also be displayed, where, for
8 example, the median value for each image would be black and
9 where positive and negative values would have a particular
10 color which, when combined would result in distinctive
11 colors for suspect impedance deviations.

12 The display shown in Figs. 14 and 15 can also be
13 utilized to show a plurality of images of the same region at
14 varying frequencies and one or more different impedance
15 measures of a given region.

16 Figs. 17A and 17B show a block diagram of a preferred
17 embodiment of a system 200 which incorporates a number of
18 multi-element probes. It should be understood that the exact
19 design of system for impedance imaging will depend on the
20 types of probes attached to the system and the exact imaging
21 modalities (as described above) which are used.

22 As shown in Figs. 17A and 17B the preferred system can
23 incorporate biopsy needle probe 154, two plate probes 28, 30
24 such as those shown in Figs. 1-3, scan zoom probe 100 such
25 as that shown in Fig. 6A, conformal probe 139 such as that
26 shown in Fig. 7B, a bra-cup probe, finger/glove probe 130
27 such as that shown in Fig. 7A, laparoscopic probe 150 such
28 as that shown in Fig. 9 or an intra-operative probe 140 as
29 shown in Fig. 8. Furthermore, when three probes are used as
30 in Fig. 11E, provision is made for attachment of a third
31 plate probe. The position of the plate and needle probes is
32 controlled by controller 181 as described in respect to Fig.
33 11D.

34 The probes as connected via a series of connectors,
35 indicated by reference numeral 302 to a selection switch 304
36 which chooses one or more of the probes in response to a

1 command from a DSP processor 306. Selection switch 304
2 switches the outputs of the probes, namely the signals
3 detected at the sensing elements of the probes (or amplified
4 versions of these signals) to a set of 64 amplifiers 308,
5 one amplifier being provided for each sensing element. For
6 those probes, such as the large plate probes, which have
7 more than 64 sensing elements, the selection switch will (1)
8 sequentially switch groups of 64 sensing elements to
9 amplifier set 308, (2) choose a subset of sensing elements
10 on a coarser grid than the actual array by skipping some
11 elements, as for example every second element, (3) sum
12 signals from adjacent elements to give a new element array
13 of lower resolution and/or (4) choose only a portion of the
14 probe for measurement or viewing. All of these switching
15 activities and decisions are communicated to the switch by
16 DSP processor 306 which acts on command from a CPU 312. The
17 output of the amplifiers is passed to a multiplexer 307
18 where the signals are serialized prior to conversion to
19 digital form by a, preferably 12-bit, A/D convertor 310. A
20 programmable gain amplifier 309, preferably providing a gain
21 which is dependent on the amplitude of the signals, is
22 optionally provided to match the signal to the range of the
23 A/D convertor. The output of A/D 310 is sent to the DSP for
24 processing as described above. In a preferred embodiment of
25 the invention DSP 306 is based on a Motorola MC 68332
26 microprocessor.

27 While 64 amplifiers has been chosen for convenience and
28 lower cost, any number of amplifiers can be used.

29 The DSP calculates the impedance results and send the
30 results to CPU 312 for display on a graphic data display 16,
31 printing on a printer 18 or other output signals generation
32 as described above by a light indicator 314 or a sound
33 indicator 316.

34 Alternatively, the DSP directs signal sampling and
35 averages together the samples or pre-processes them, sending
36 the averaged or pre-processed samples to CPU 312, which then

1 performs the impedance calculations.

2 The CPU may also receive images from video camera 256,
3 for example, when used with an intra-operative probe, from
4 an endoscopic optics and camera system 320, for example when
5 the camera views the outer surface of the laparoscopic probe
6 or from an ultra sound imager 322, for example, in biopsy
7 performance as shown in Figs. 11A and 11B. When an image is
8 acquired from one of these cameras a frame grabber 324 is
9 preferably provided for buffering the camera from the CPU.
10 As described above, the CPU combines these images with the
11 impedance images provided by one or more probes for display
12 or other indication to the operator.

13 Fig. 15 also shows a programmable reference signal
14 generator 326 which receives control and timing signals from
15 the DSP. The reference signal generator generates excitation
16 signals which are generally supplied, during impedance
17 imaging, to reference probe 13, which, as described above,
18 is placed at a point (or at more than one point) on the body
19 remote from the region of impedance measurement. Signal
20 generator 312 may produce a sinusoidal waveform, pulses or
21 spikes of various shapes (including a bipolar square shape)
22 or complex polychromatic waveforms combining desired
23 excitation frequencies. Appropriate impedance calculations,
24 in DSP 306 or in CPU 312, are implemented in accordance with
25 the waveform of the excitation.

26 Where a breast is imaged and one of the two plates is
27 used as the source of excitation, as described above, the
28 output of signal generator is sent to the exciting plate
29 (signal paths not shown for simplicity). A current overload
30 sensor 330 is preferably provided after the signal generator
31 to avoid overloads caused by short circuits between the
32 reference probe and the imaging probe or ground.

33 Also shown on Fig. 17A is an internal calibration
34 reference 332 which is preferably used for internal
35 calibration of the system and for testing and calibration of
36 the probes.

1 For internal testing and calibration, calibration
2 reference 232 receives the signals generated by the
3 programmable reference signals generator as passed to the
4 selection switch, in series with an internal admittance in
5 the calibration reference, as selected by the DSP processor.
6 The DSP processor computes the admittance from signals
7 received from the A/D convertor and compares the computed
8 admittance with the actual admittance provided by internal
9 calibration reference 332. This comparison can be provide an
10 indication that the system requires adjustment or repair or
11 can be used to calibrate the system.

12 Similarly, the output of calibration reference 332 may
13 be provided to probe cover 88 for calibration and quality
14 assurance of a plate or scan probe as described above. Under
15 this situation, the DSP instructs selection switch 304 to
16 choose the input from the respective probe.

17 Also provided is a user interface 334 such as a
18 keyboard, mouse, joystick or combinations thereof, to allow
19 the operator to enter positional information via the screen
20 and to choose from among the probes provided and from the
21 many options of calculation, display, etc.

22 Although described together as the preferred embodiment
23 of the invention, it is not necessary to use the probes of
24 the invention, the methods of calculation of impedance and
25 impedance characteristics of the invention and the preferred
26 apparatus of the invention together. While it is presently
27 preferred that they be used together they may each be used
28 with probes, calculation methods and apparatus for impedance
29 imaging as applicable and as available.

30 Certain aspects of the invention have been described
31 with respect to a biopsy needle or with respect to placement
32 of such a needle. It should be understood that such
33 description and aspects of the invention are equally
34 applicable to positioning needles, catheters, endoscopes,
35 etc.

36 Although various embodiments, forms and modifications

1 have been shown, described and illustrated above in some
2 detail in accordance with the invention, it will be
3 understood that the descriptions and illustrations are by
4 way of example, and that the invention is not limited
5 thereto but encompasses all variations, combinations and
6 alternatives falling within the scope of the claims which
7 follow:

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1

C L A I M S

2 1. A multi-element probe for providing an electrical
3 connection to a tissue surface comprising:

4 a plurality of individual conductive sensing elements,
5 each having a front portion suitable for contact with
6 the tissue surface;

7 a plurality of conductive elements providing an
8 electrical connection to the respective individual sensing
9 elements; and

10 a partition separating the individual sensing elements
11 such that when the individual probes contact the tissue
12 surface they are substantially electrically isolated from
13 each other.

14

15 2. A probe according to claim 1 wherein the sensing
16 elements comprise a conductive, viscous gel.

17

18 3. A probe according to claim 1 wherein the sensing
19 elements comprise a conductive, flexible, solid.

20

21 4. A probe according to claim 1 wherein the sensing
22 elements comprise a sponge impregnated with a
23 conductive viscous gel.

24

25 5. A probe according to claim 1 wherein each individual
26 sensing element is located in a well formed by the partition
27 and a substrate underlying the sensing element.

28

29 6. A probe according to claim 5 wherein the side of the
30 substrate opposite the sensing elements is formed with an
31 alignment structure for aligning the multi-element probe.

32

33 7. A probe according to claim 5 wherein the well is formed
34 by embossing the partition on a sheet of material, whereby
35 the un-embossed portion of the sheet forms the substrate
36 underlying the sensing element.

1 8. A probe according to claim 6 wherein the well is formed
2 by embossing the partition on a sheet of material, whereby
3 the un-embossed portion of the sheet forms the substrate
4 underlying the sensing element and wherein the indentations
5 are the back of the embossed wells.

6

7 9. A probe according to claim 5 wherein the well is formed
8 by laminating a grid formed by holes punched in a sheet or
9 formed by extrusion to the substrate.

10

11 10. A probe according to claim 5 wherein the well is formed
12 by printing the partitions onto the substrate.

13

14 11. A probe according to claim 5, including an electrical
15 connection between a first surface of the substrate inside
16 the well and a second, opposite, surface of the substrate.

17

18 12. A probe according to claim 11 and also comprising an
19 anisotropic conductive sheet overlying the second surface of
20 the substrate.

21

22 13. A probe according to claim 11 and also comprising a
23 conductive contact on the second surface of the substrate
24 which is electrically connected to the first surface of the
25 substrate and an adhesive contact overlying the conductive
26 contact.

27

28 14. A probe according to claim 1 wherein the sensing
29 elements do not extend past the top of the partition.

30

31 15. A probe according to claim 14 wherein the sensing
32 elements do not extend to the top of the partition.

33

34 16. A probe according to any of the preceding claims and
35 including a cover having a conductive surface facing the
36 front portion of the sensing elements.

1

2 17. A multi-element probe for providing an electrical
3 connection to tissue comprising:

4 a plurality of individual conductive sensing elements,
5 each having a front portion suitable for contact with the
6 tissue;

7 a plurality of conductive elements providing an
8 electrical connection to the respective individual sensing
9 elements; and

10 a cover having a surface facing the front portion of
11 the sensing elements, at least that portion of said surface
12 facing the sensing elements being an electrically conductive
13 surface.

14

15 18. A multi-element probe according to claim 17 wherein
16 said cover is formed of a flexible material and wherein, in
17 an unstressed position said electrical conductive surface
18 does not contact said conductive sensing elements.

19

20 19. A multi-element probe according to claim 18 wherein
21 said cover is so configured that the surface contacts the
22 sensing elements when a surface of the cover opposite the
23 conductive surface is pressed toward the sensing elements.

24

25 20. A multi-element probe according to claim 17 wherein the
26 cover also includes an area, on the surface facing the
27 individual sensing elements, remote from the individual
28 sensing elements, which is a conductive area electrically
29 connected to said portions facing the sensing elements, the
30 multi-element probe also including a contact electrically
31 connected to the exterior of the probe.

32

33 21. A multi-element probe according to claim 20 wherein, in
34 an unstressed position, said electrical conductive surface
35 does not contact said contact and wherein said cover is so
36 configured that the conductive area contacts the contact

1 when a surface of the cover opposite the conductive surface
2 is pressed toward the sensing elements.

3

4 22. A multi-element probe according to claim 17 and further
5 comprising at least one contact suitable for connection to
6 an external source of electrical energy and also including
7 impedance elements between the conductive surfaces opposite
8 the sensing elements and the contact.

9

10 23. A multi-element probe according to claim 20 and also
11 including impedance elements between the conductive surfaces
12 opposite the sensing elements and the contact.

13

14 24. A multi-element probe for providing an electrical
15 connection to a tissue surface comprising:

16 a plurality of individual conductive sensing elements,
17 each having a front portion suitable for contact with the
18 tissue surface; and

19 a plurality of conductive elements providing an
20 electrical connection to the respective individual sensing
21 elements,

22 wherein the side of the substrate opposite the sensing
23 elements is formed with indentations for aligning the multi-
24 element probe.

25

26 25. A multi-element probe for the measurement of impedance
27 of tissue, wherein the elements of the probe are
28 sufficiently transparent to allow visualization of tissues
29 beneath the probe when the probe is placed in contact with
30 the tissues.

31

32 26. A multi-element probe for providing an electrical
33 connection to a tissue surface comprising:

34 a plurality of individual conductive sensing elements,
35 each having a front portion suitable for contact with the
36 tissue surface; and

1 a plurality of conductive elements providing an
2 electrical connection to the respective individual sensing
3 elements, wherein

4 the probe is sufficiently transparent to allow
5 visualization of tissues beneath the probe when the probe is
6 placed in contact with the tissues.

7

8 27. A multi-element probe according to any of claims 1-16
9 or 17-26, wherein the sensing elements are formed of a
10 spongy conductive material.

11

12 28. A multi-element probe for providing an electrical
13 connection to a tissue surface comprising:

14 a plurality of individual conductive sensing elements,
15 each having a front portion suitable for contact with the
16 tissue surface; and

17 a plurality of conductive elements providing an
18 electrical connection to the respective individual sensing
19 elements,

20 wherein the sensing elements are formed of a spongy
21 conductive material.

22

23 29. A multi-element probe according to any of claims 1-16,
24 17-26 or 28 wherein the sensing elements are formed on a
25 flexible surface, whereby the multi-element probe conforms,
26 at least in part, to the tissue.

27

28 30. A multi-element probe according to any of claims 1-16,
29 17-26 or 28, wherein the probe is provided with apertures
30 between sensing elements suitable for the passage of a thin
31 elongate object.

32

33 31. A multi-element probe for providing an electrical
34 connection to a tissue surface comprising:

35 a plurality of individual conductive sensing elements,
36 each having a front portion suitable for contact with the

1 tissue surface; and
2 a plurality of conductive elements providing an
3 electrical connection to the respective individual sensing
4 elements,
5 wherein the probe is provided with apertures between
6 sensing elements suitable for the passage of a thin elongate
7 object.
8
9 32. A multi-element probe for providing an electrical
10 connection to a tissue surface comprising:
11 an array of individual conductive sensing elements
12 spaced over a surface, each element having a front portion
13 suitable for contact with the tissue surface; and
14 a plurality of conductive elements providing an
15 electrical connection to the respective individual sensing
16 elements,
17 wherein the area of the conductive elements comprises
18 less than 70% of the total area encompassed by the array.
19
20 33. A multi-element probe according to any of claims 1-16,
21 17-26, 28, 31 or 32, wherein at least a portion of the
22 surface of the probe facing the tissue to be measured is
23 adhesive to the tissue.
24
25 34. A multi-element probe for providing an electrical
26 connection to a tissue surface comprising:
27 a plurality of individual conductive sensing elements,
28 each having a front portion suitable for contact with the
29 tissue surface; and
30 a plurality of conductive elements providing an
31 electrical connection to the respective individual sensing
32 elements,
33 wherein at least a portion of the surface of the probe
34 facing the tissue to be measured is adhesive to the tissue.
35
36 35. A multi-element probe according to any of claims 1-16,

1 17-26, 28, 31, 32 or 34, and including:

2 means for attaching the probe to the finger of a
3 person whereby the person can perform palpative examination
4 concurrently with impedance imaging.

5

6 36. A multi-element probe for providing an electrical
7 connection to a tissue surface comprising:

8 a plurality of individual conductive sensing elements,
9 each having a front portion suitable for contact with the
10 tissue surface; and

11 a glove having fingers, said sensing elements being
12 attached to the outside of one of the glove at one of the
13 fingers whereby a wearer of the glove can perform palpative
14 examination concurrently with impedance imaging.

15

16 37. A multi-element intermediate device for providing an
17 electrical connection between a multiconductor sensor device
18 and a tissue surface comprising a plurality of individual
19 conductive sensing elements, substantially electrically
20 insulated from each other, each having a front portion
21 suitable for contact with the tissue surface and a back
22 portion detachably matable to the multi-conductor sensor
23 device.

24

25 38. An intermediate device according to claim 37 and
26 including electrical contacts on the back portion which are
27 electrically connected to the sensing element and which
28 contact a plurality of mating contacts on the multi-
29 conductor sensor device.

30

31 39. A multi-element intermediate device for providing an
32 electrical connection between a multiconductor sensor device
33 and a tissue surface comprising:

34 a multi-element probe according to any of claims 1-15,
35 17-26, 28, 31, 32 or 34, and having a back portion
36 detachably matable to the multi-conductor sensor device.

1 40. An intermediate device according to claim 39 and
2 including electrical contacts on the back portion which are
3 electrically connected to the sensing element and which
4 contact a plurality of mating contacts on the multi-
5 conductor sensor device.

6

7 41. A catheter or endoscopic probe comprising:
8 a multi-element probe according to any of claims 1-16,
9 17-26 or 28; and

10 a fiber optic viewer whose field of view includes at
11 least one surface of the probe when the probe is in contact
12 with the tissue.

13

14 42. A catheter or endoscopic probe comprising:
15 a multi-element probe for providing an electrical
16 connection to a tissue surface, the probe including a
17 plurality of individual conductive sensing elements on a
18 substrate, each sensing element having a front portion
19 suitable for contact with the tissue surface and fiduciary
20 marks visible from an other surface; and
21 a fiber optic viewer whose field of view includes at
22 least the other surface of the probe.

23

24 43. Apparatus for impedance imaging of a breast comprising:
25 a multi-element probe comprising a plurality of sensing
26 elements and adapted for mounting on one side of a breast;
27 an electrode adapted for mounting on a side of the
28 breast substantially opposite the multi-element probe; and
29 a source of electrical energy which provides a voltage
30 between at least a portion of the electrode and at least one
31 element of the probe.

32

33 44. Apparatus for impedance imaging of a breast comprising:
34 a multi-element probe comprising a plurality of sensing
35 elements and adapted for mounting on one side of a breast;
36 an electrode adapted for mounting on a side of the

1 breast substantially opposite the multi-element probe;
2 an additional electrode adapted for mounting on portion
3 of the body remote from the breast; and
4 a source of electrical energy which provides a voltage
5 between the additional electrode and at least one element of
6 the probe.

7

8 45. Apparatus according to claim 43 or claim 44 wherein the
9 multi-element probe and the electrode adapted for mounting
10 on a side of the breast form respective parallel planes.

11

12 46. Apparatus according to claim 43 or claim 44 wherein the
13 multi-element probe and the electrode adapted for mounting
14 on a side of the breast form two planes at an angle to each
15 other.

16

17 47. Apparatus according to claim 43 or claim 44 and
18 including a plurality of receivers which measure an
19 electrical signal at the sensing elements.

20

21 48. Apparatus according to claim 43 or claim 44 wherein the
22 electrode adapted for mounting on a side of the breast
23 comprises a second multi-element probe.

24

25 49. Apparatus according to claim 43 wherein the multi-
26 element probe comprises a multi-element probe according to
27 any of claims 1-16, 17-26, 28, 31, 32 or 34.

28

29 50. Apparatus according to claim 49 wherein at least one of
30 the multi-element probes is rigid and non-planar in
31 accordance with the shape of a body structure.

32

33 51. Apparatus according to claim 49 wherein at least one of
34 the multi-element probes is flexible so as to conform to the
35 shape of a body structure.

36

- 1 52. Apparatus for impedance imaging of a breast comprising:
2 a first multi-element probe comprising a plurality of
3 sensing elements and adapted for mounting on one side of a
4 breast;
5 a second multi-element probe adapted for mounting on a
6 side of the breast substantially opposite the multi-element
7 probe; and
8 a source of electrical energy which alternatively
9 energizes at least some of the elements of one or the other
10 of the first and second multi-element probes by supplying a
11 voltage thereto, wherein the unenergized one of the multi-
12 element probes forms an image based on the voltage applied
13 to the energized probe.
- 14
- 15 53. Apparatus according to claim 52 wherein the first and
16 second multi-element probes form respective parallel planes.
- 17
- 18 54. Apparatus according to claim 52 wherein the first and
19 second multi-element probes form two planes at an angle to
20 each other.
- 21
- 22 55. Apparatus according to any of claims 52-54 and
23 including a plurality of receivers which measure an
24 electrical signal at the sensing elements.
- 25
- 26 56. Apparatus according to claim 52 wherein the multi-
27 element probe comprises a multi-element probe according to
28 any of claims 1-16, 17-26, 28, 31, 32 or 34.
- 29
- 30 57. Apparatus for impedance imaging of tissue comprising:
31 an impedance probe which produces signals
32 representative of impedance values below the elements and
33 having fiduciary marks which are visible when the probe
34 contacts the tissue;
35 an impedance image generator which receives the signals
36 and produces an impedance image;

1 a video camera which views the probe and tissue and
2 generates a video image; and

3 a video image processor which receives a video image of
4 the tissue without the probe in place and an image of the
5 tissue with the probe in place, and provides a video image
6 of the tissue with the fiduciary marks and impedance image
7 superimposed thereon.

8

9 58. A method of impedance imaging of a region of the body
10 comprising:

11 (a) positioning a multi-element probe, comprising a
12 plurality of sensing elements, on one side of the region;

13 (b) positioning an electrode on a side of the region
14 substantially opposite the multi-element probe;

15 (c) electrifying the electrode; and

16 (d) measuring a signal at at least some of the elements
17 of the multi-element probe.

18

19 59. A method of impedance imaging of a region of the body
20 comprising:

21 (a) positioning a multi-element probe, comprising a
22 plurality of sensing elements, on one side of the region;

23 (b) positioning an electrode on a side of the region
24 substantially opposite the multi-element probe;

25 (c) positioning a second electrode on a portion of the
26 body;

27 (d) electrifying the second electrode; and

28 (e) measuring a signal at at least some of the elements
29 of the multi-element probe.

30

31 60. A method according to claim 58 or claim 59 wherein (b)
32 comprises positioning a second multi-element probe on a side
33 of the region substantially opposite the multi-element
34 probe.

35

36 61. A method of impedance imaging of a region of the body

1 comprising:

2 positioning a first multi-element probe, comprising a
3 plurality of sensing elements, on one side of the region;
4 positioning a second multi-element probe on a side of
5 the region substantially opposite the multi-element probe;
6 electrifying fewer than all of the plurality of
7 sensing elements of the second multi-element probe; and
8 measuring a signal at at least some of the elements of
9 the first multi-element probe.

10

11 62. A method of impedance imaging of a region of the body
12 comprising:

13 contacting one side of the region with a first multi-
14 element probe, comprising a first plurality of sensing
15 elements;

16 contacting a second side of the region with a second
17 multi-element probe, comprising a second plurality of
18 sensing elements;

19 receiving signals from said first and second multi-
20 element probes in response to a stimulus; and

21 combining the signals received from both probes to
22 locate objects within the region.

23

24 63. A method for guidance in the placement of an elongate
25 element in a region of a subject comprising:

26 (a) inserting the elongate element into tissue, said
27 element including a plurality of impedance measuring sensing
28 elements thereon;

29 (b) measuring the impedance between the plurality of
30 sensing elements and an electrode in contact with the
31 subject; and

32 (c) guiding the element to a desired position having
33 defined impedance properties in response to measurements of
34 impedance made in (b).

35

36 64. A method according to claim 63 and also including;

1 imaging the region of the subject including the
2 elongate element and generating an image thereof;
3 receiving the image and the measurements of impedance
4 made in (b) and superimposing a representation of the
5 impedance measurements on the image of the elongate element
6 and surrounding tissues; and
7 displaying said superimposed images.

8

9 65. A method according to claim 64 wherein the outer
10 surface of the elongate element is formed with a matrix of
11 impedance measuring elements each measuring the tissue
12 impedance in a direction generally perpendicular to the
13 element and wherein the display indicates a guiding
14 direction for the elongate element based on the impedance
15 measurements.

16

17 66. A method according to any of claims 63-65 wherein the
18 elongate element is inserted into the body through a hole in
19 an array of impedance probe elements and including:

20 providing a two-dimensional impedance image based on
21 signals received by the array;

22 guiding the elongate element based on the two-
23 dimensional image; and

24 determining the desired depth of the elongate element
25 based on impedance signals received from the impedance
26 measuring elements on the elongate element.

27

28 67. A method for guidance in the placement of an elongate
29 element in portion of a patient comprising:

30 forming a first two-dimensional impedance image of at
31 least a part of said portion from a given direction;

32 forming a second two dimensional impedance image of at
33 least a part of the portion using a multi-element impedance
34 probe placed at a known angle to the plane of the first
35 image;

36 inserting the elongate element between elements of the

1 multi-element probe; and
2 guiding the elongate element to a point of impedance
3 deviation at least partially under the guidance of the first
4 and second two dimensional images.

5

6 68. A method comprising:
7 providing an impedance measurement system including a
8 multi-element probe attached to at least one finger of an
9 examiner; and

10 providing an indication of impedance generated on the
11 basis of signals detected by said elements, whereby both a
12 tactile and impedance indication of an examined tissue are
13 simultaneously acquired.

14

15 69. A method for improving the sensitivity of impedance
16 imaging comprising:

17 contacting tissue with a multi-element probe;
18 contacting a different portion of tissue with at least
19 one electrode;

20 exciting the at least one electrode with a pulsed
21 voltage;

22 measuring signals, responsive to said pulsed voltage at
23 at least a plurality of the elements of the probe;

24 computing the real and imaginary parts of an admittance
25 represented by said voltage and signals for a plurality of
26 frequencies at a plurality of said elements; and

27 choosing at least one frequency as a measurement
28 frequency which gives a large difference for said measures
29 at different elements of the probe.

30

31 70. A method for identifying, in a multi-element impedance
32 probe which forms an impedance map of tissue when placed on
33 the surface thereof, artifacts among impedance deviations
34 from the surroundings, the method comprising:

35 manipulating the tissue underlying the probe while the
36 probe remains in stationary contact with the surface of the

1 tissue; and

2 identifying as a non-artifact those impedance
3 deviations which shift in the direction of the manipulation
4 on the impedance map.

5

6 71. A method for identifying, in a multi-element impedance
7 probe which forms an impedance map of tissue when placed on
8 the surface thereof, artifacts among impedance deviations
9 from the surroundings, the method comprising:

10 moving the probe along the surface of the tissue; and
11 identifying as an artifact those impedance deviations
12 which remain stationary or disappear in the impedance map as
13 the probe is moved.

14

15 72. A method for identifying, in a multi-element impedance
16 probe which forms an impedance map of tissue when placed on
17 the surface thereof, artifacts among impedance deviations
18 from the surroundings, the method comprising:

19 moving the probe together with the tissue; and
20 identifying as a fixed artifact those impedance
21 deviations which move on the impedance map, in the opposite
22 direction from the movement of the probe and the tissue.

23

24 73. A method of displaying impedance imaging information
25 comprising:

26 displaying at least one impedance image of a region;
27 and

28 displaying an indication of the imaged region on a
29 representation of the physiology of the patient.

30

31 74. A method of displaying according to claim 73 and
32 including:

33 simultaneously displaying both a capacitance and a
34 conductance map of the same region.

35

36 75. A method of displaying impedance imaging information

1 comprising:

2 displaying a capacitance map of a region; and
3 simultaneously displaying a conductance map of the same
4 region.

5

6 76. A method of displaying impedance imaging information
7 comprising:

8 computing maps of a plurality of imaging measures; and
9 simultaneously displaying the measures.

10

11 77. A method of displaying impedance information
12 comprising:

13 computing a plurality of maps of at least one imaging
14 measure at a plurality of frequencies; and
15 simultaneously displaying the maps.

16

17 78. A method of identifying a suspected carcinoma
18 comprising:

19 comparing a capacitance map of a region to a
20 conductance map of the same region;

21 identifying a deviation from the surroundings as a
22 suspected cancer if at some frequency less than about 10 kHz
23 both the capacitance value and the conductance value are
24 higher than that of the surroundings.

25

26 79. A method of identifying a suspected atypical
27 hyperplasia comprising:

28 comparing a capacitance map of a region to a
29 conductance map of the same region;

30 identifying a deviation from the surroundings as a
31 suspected cancer if at some frequency less than 10 kHz both
32 the capacitance value and the conductance value are higher
33 than that of the surroundings.

34

35 80. A method of differentiating a suspected carcinoma from
36 a suspected atypical hyperplasia comprising:

1 comparing a capacitance map of a region to a
2 conductance map of the same region;

3 classifying a deviation from the surroundings as a
4 suspected atypical hyperplasia if at some frequency less
5 than 10 kHz the capacitance value is lower than that of the
6 surroundings and the conductance value is higher than that
7 of the surroundings; and

8 classifying a deviation from the surroundings as a
9 suspected cancer if at some frequency less than 10 kHz both
10 the capacitance value and the conductance value are higher
11 than that of the surroundings.

12

13 81. A method according to any of claims 78 to 80 wherein
14 the frequency at which the comparison of the capacitance and
15 conductance values take place is below 2500 Hz.

16

17 82. A method according to any of claims 78 to 80 wherein
18 the frequency at which the comparison of the capacitance and
19 conductance values take place is below 500 Hz.

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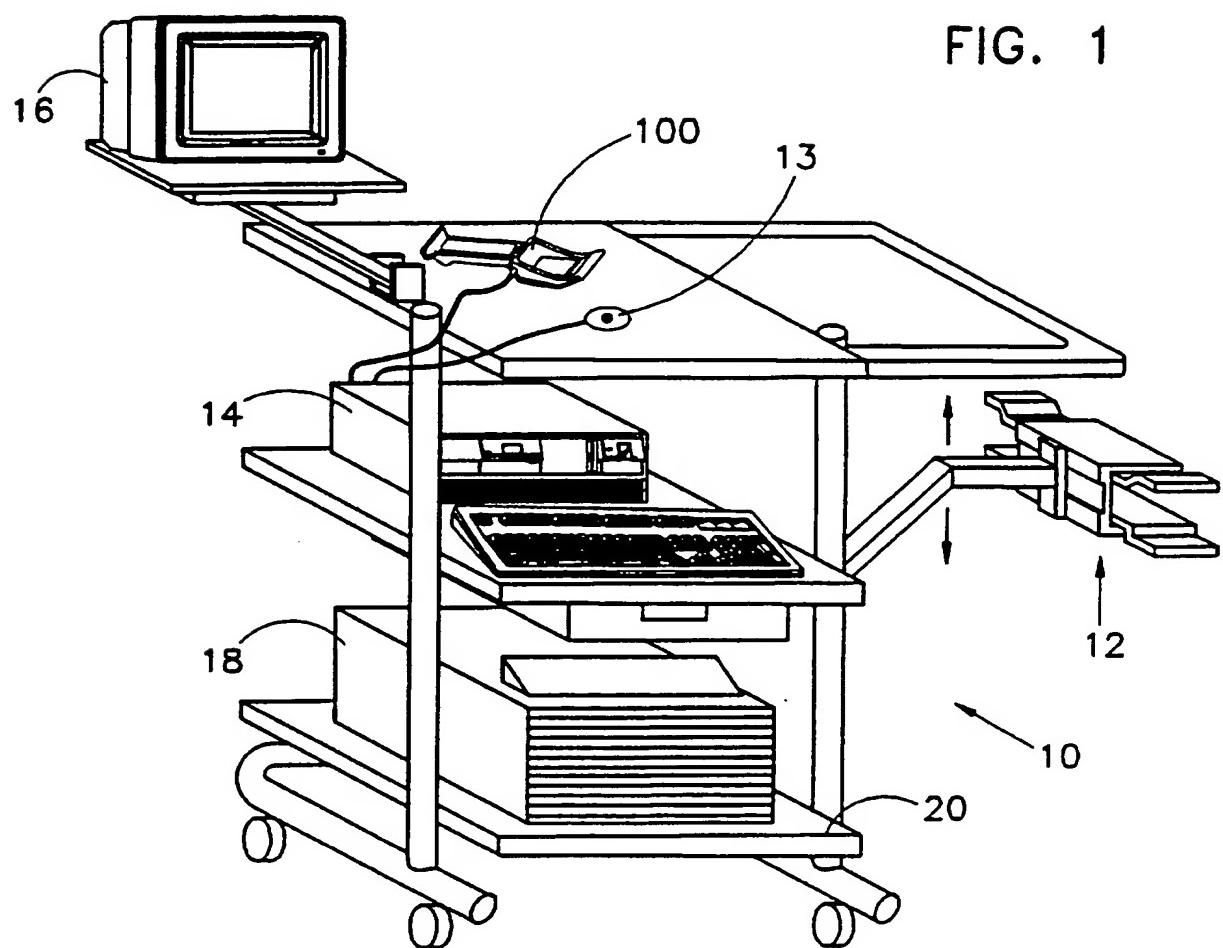
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36

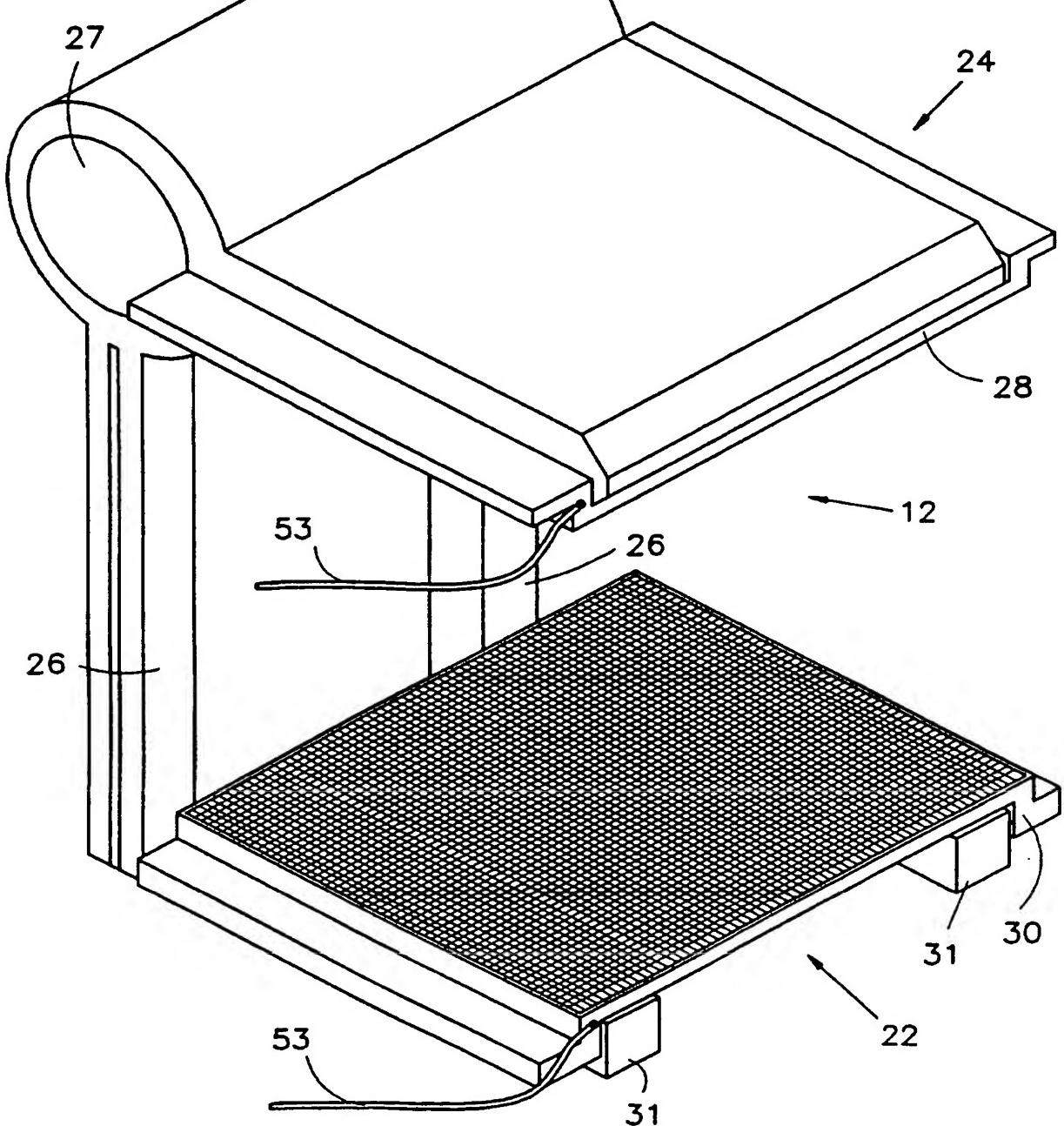
1/22

FIG. 1



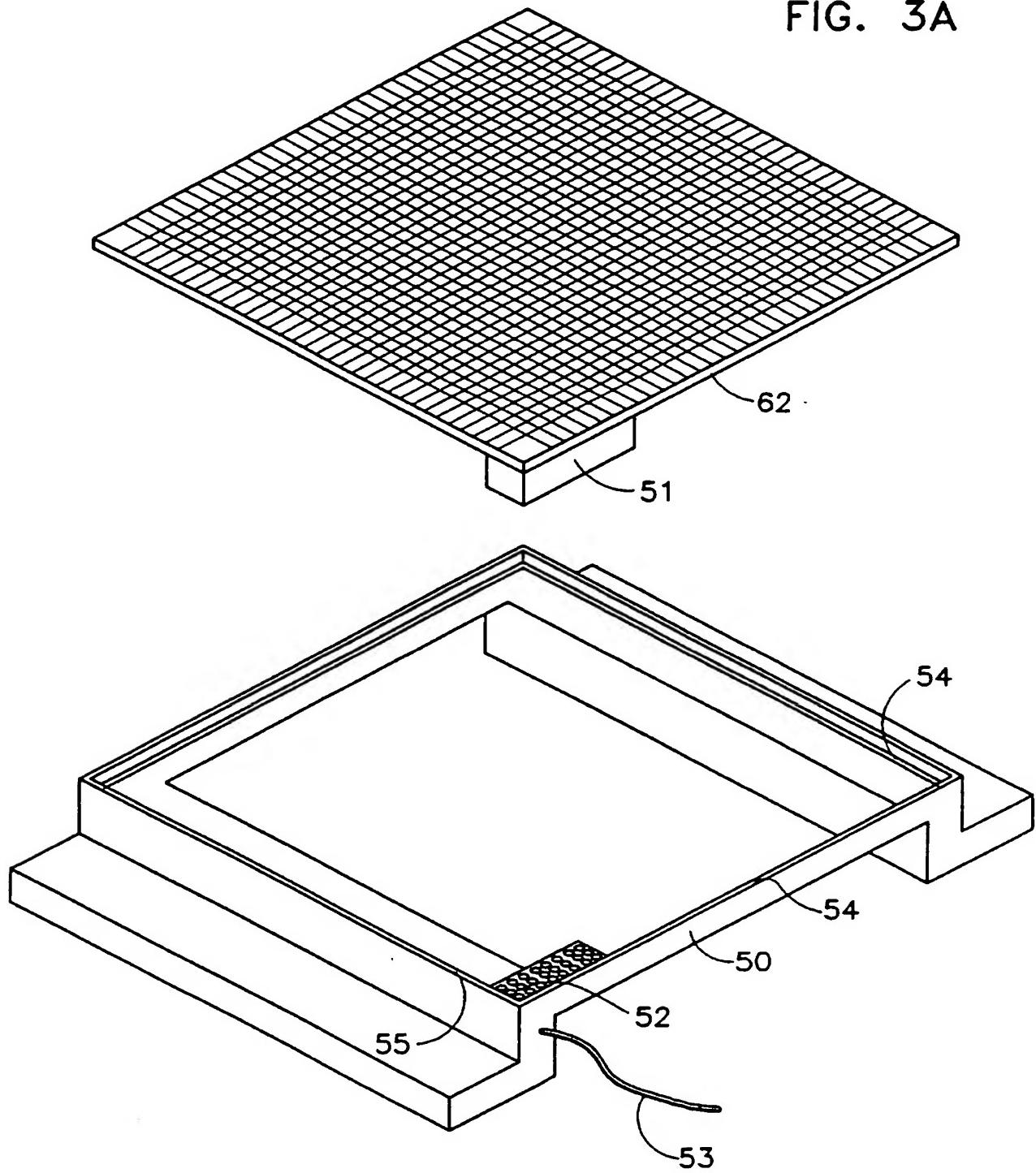
2/22

FIG. 2



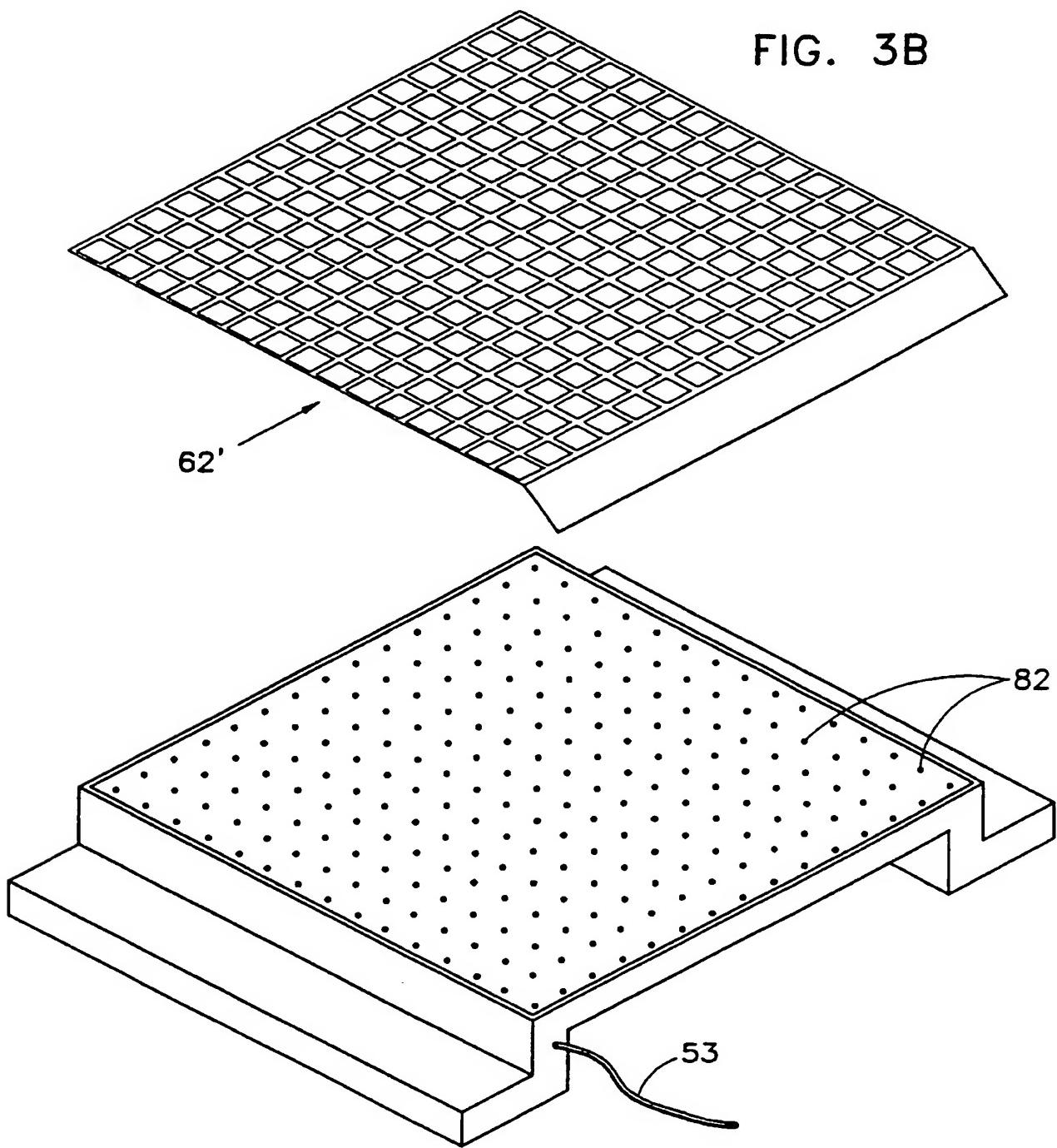
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FIG. 3A



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FIG. 3B



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FIG. 4

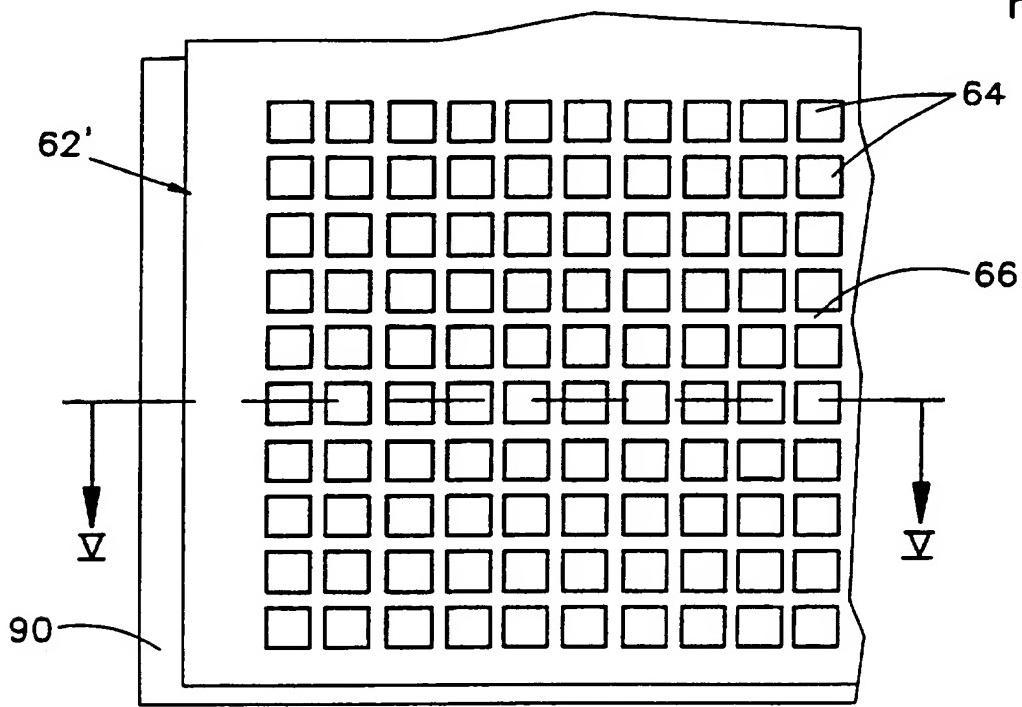
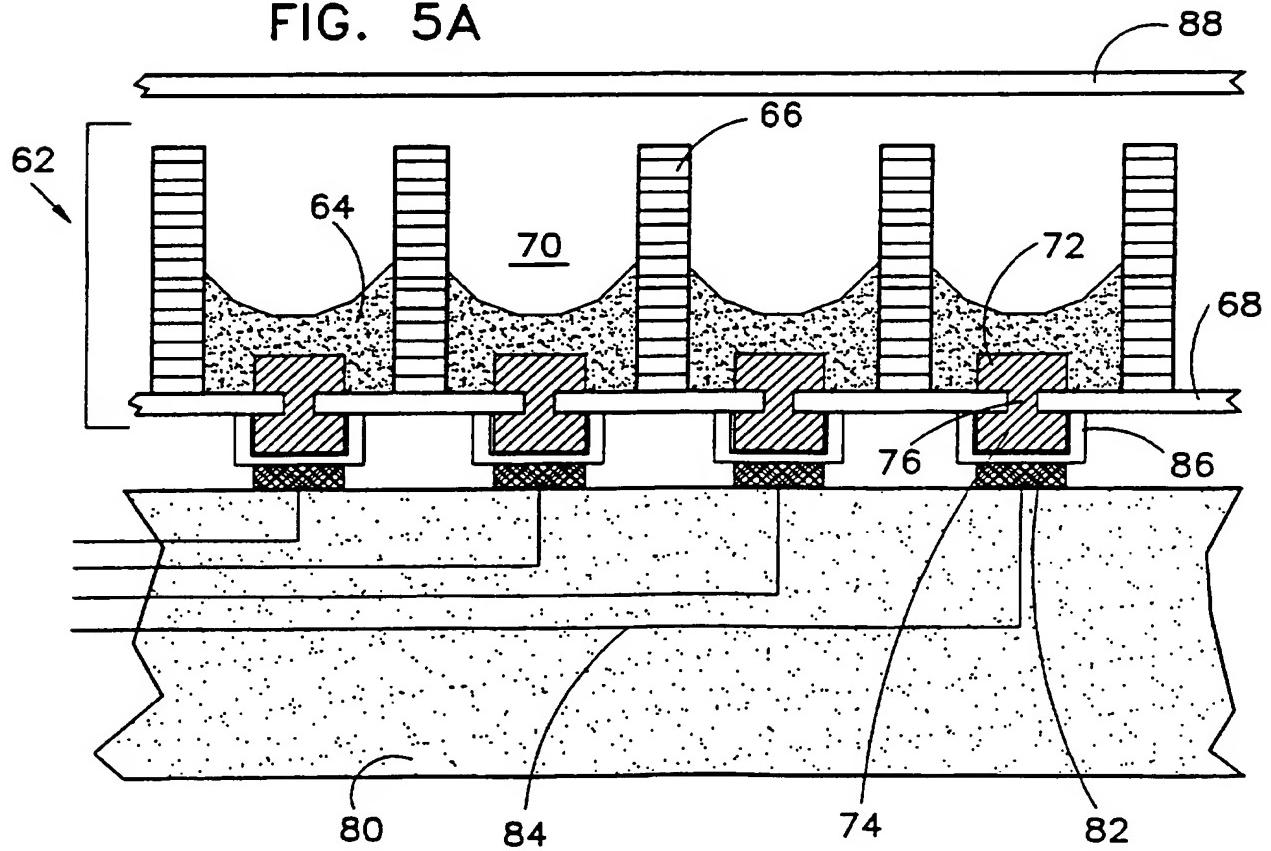
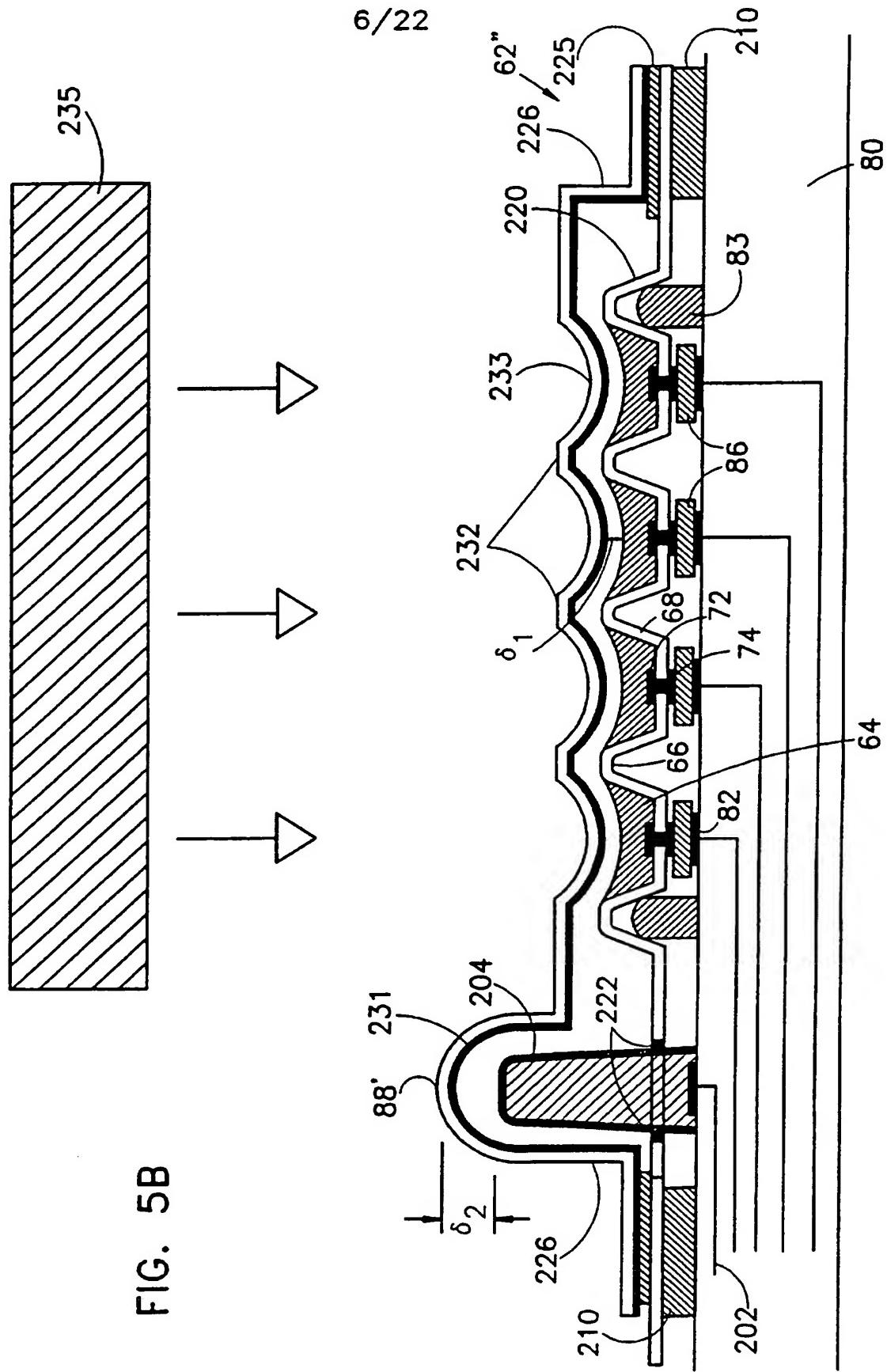


FIG. 5A

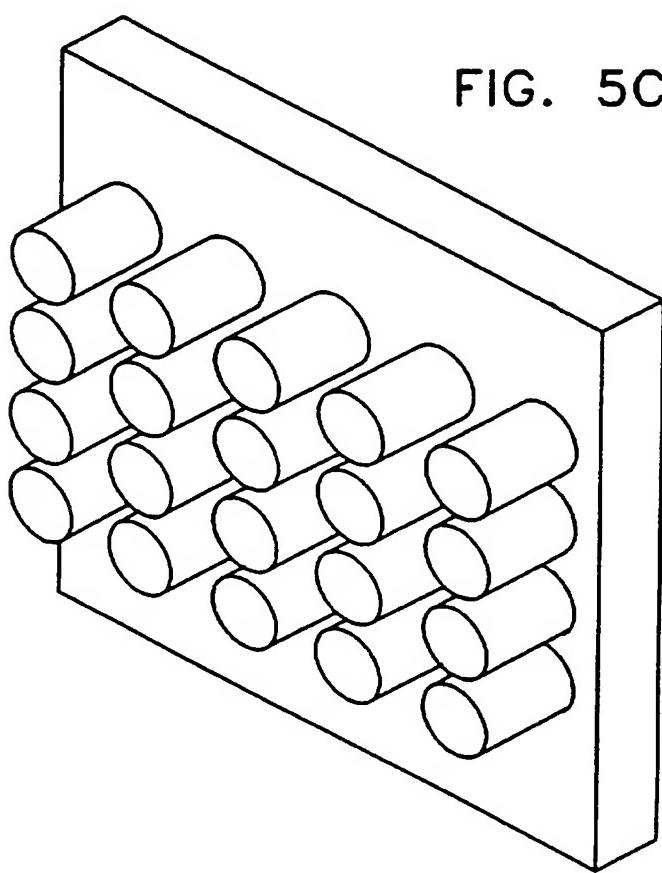


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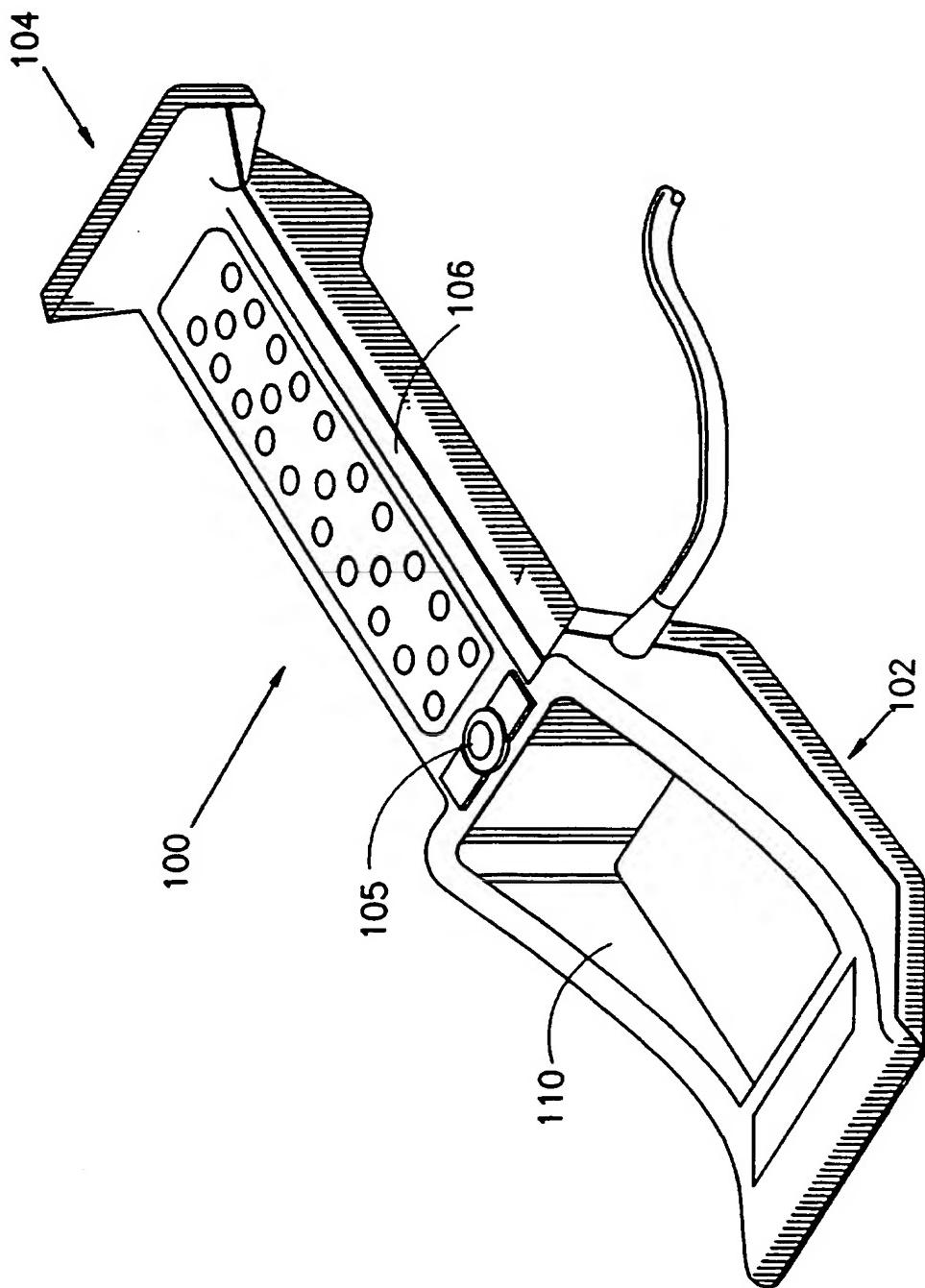
7\22

FIG. 5C



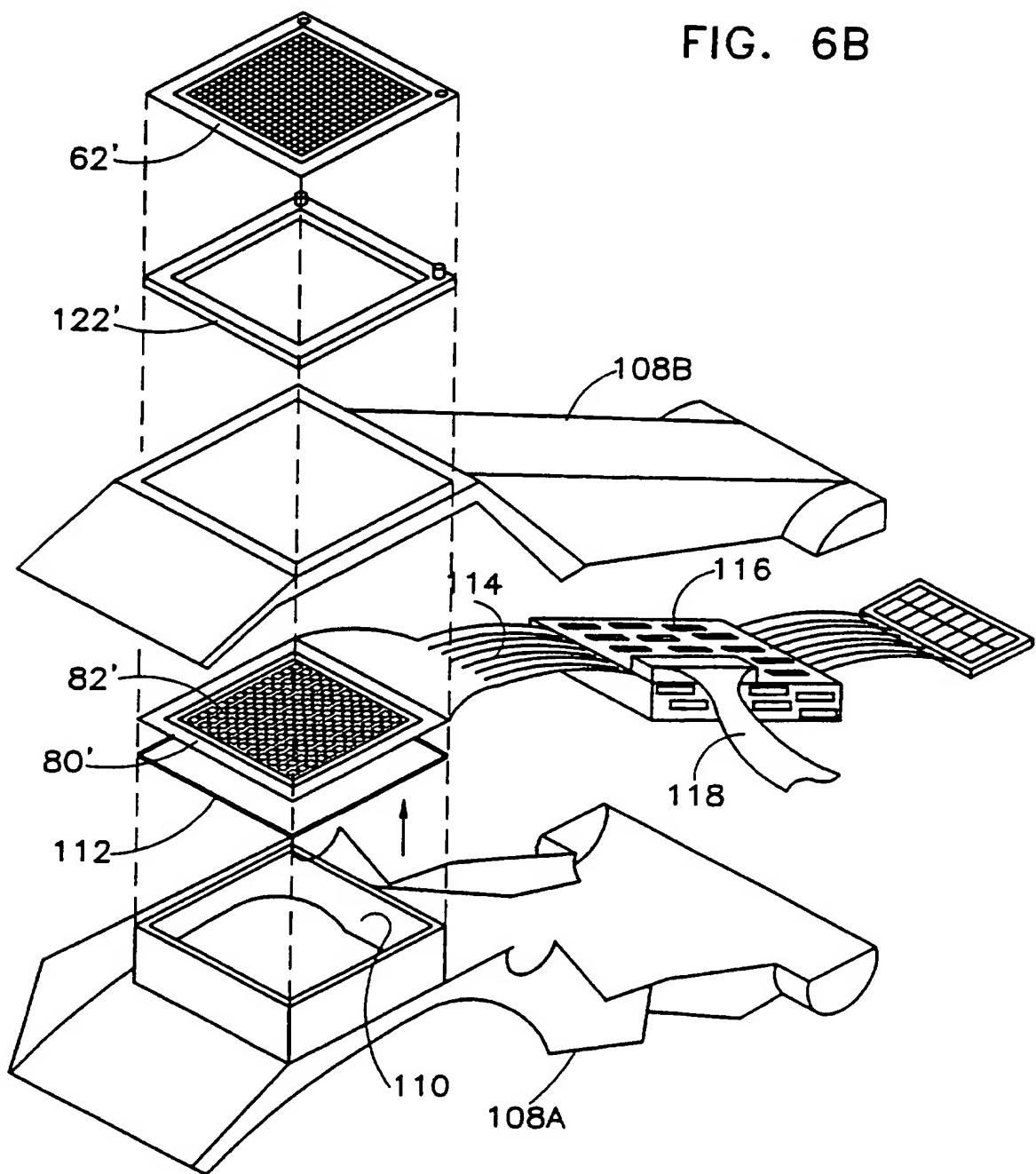
8/22

FIG. 6A



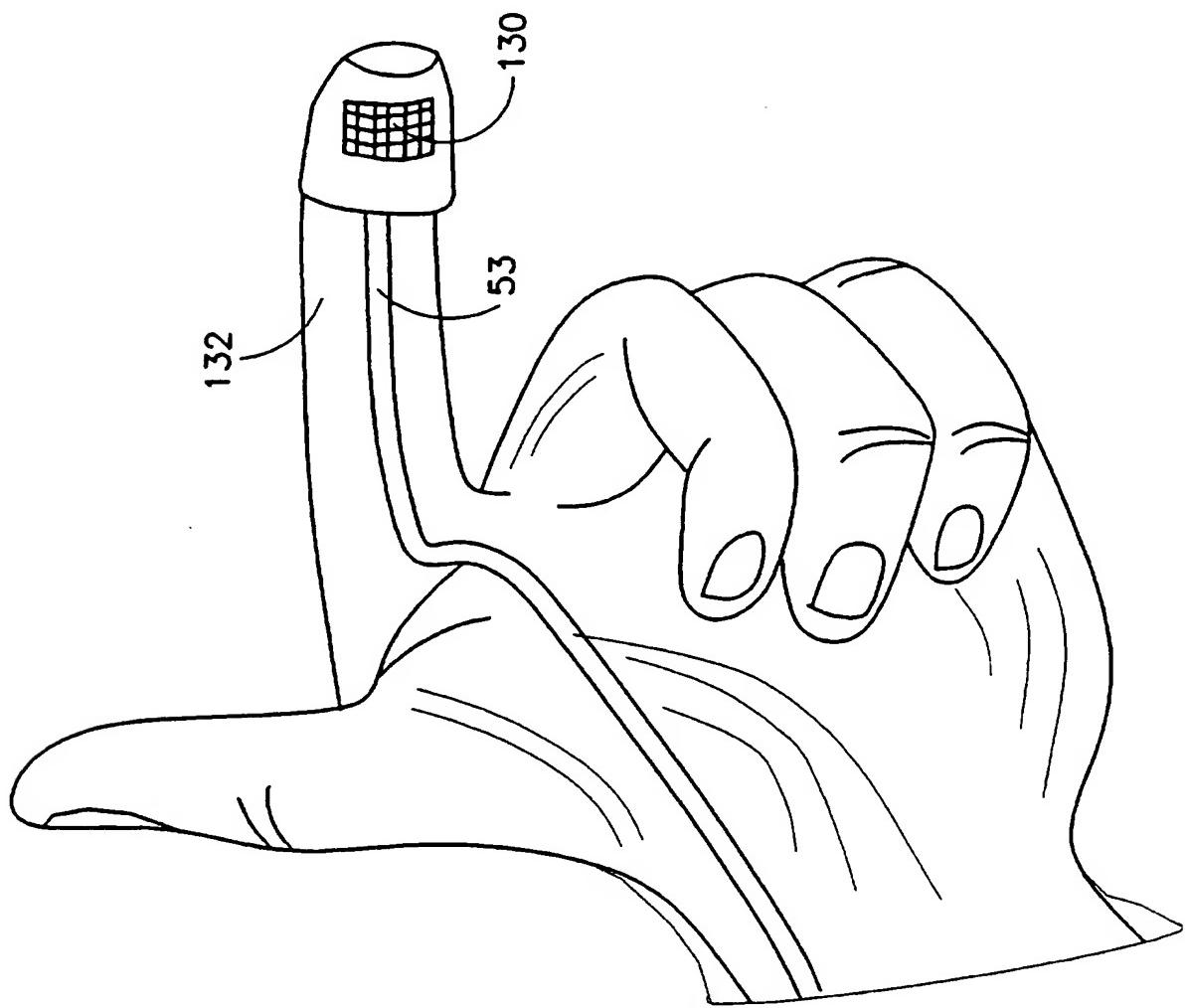
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FIG. 6B



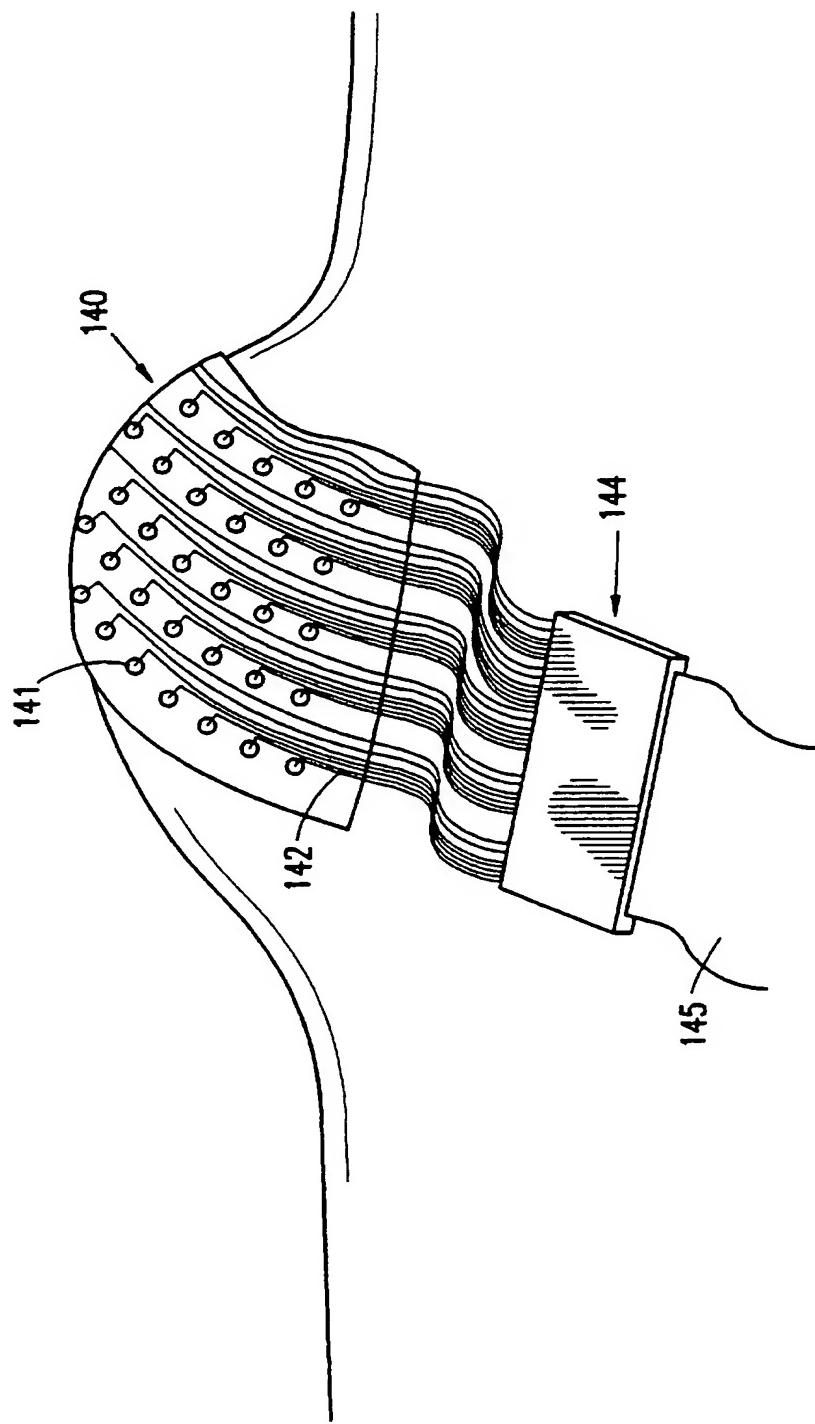
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FIG. 7A



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FIG. 7B



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FIG. 10

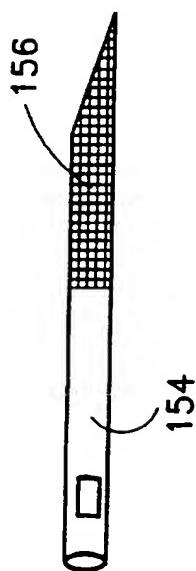


FIG. 8

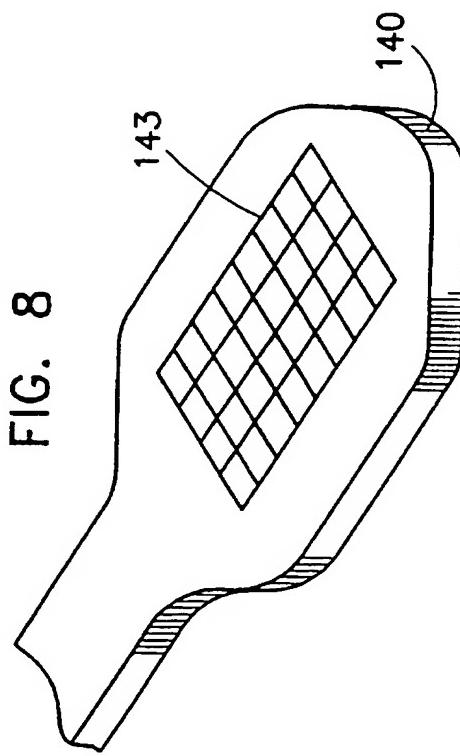
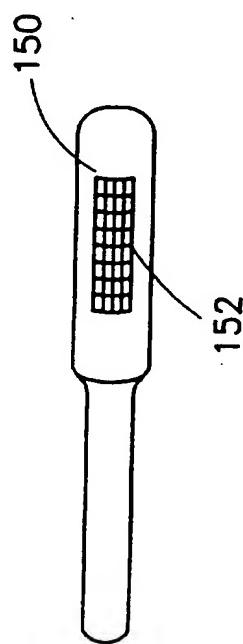


FIG. 9



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FIG. 11A

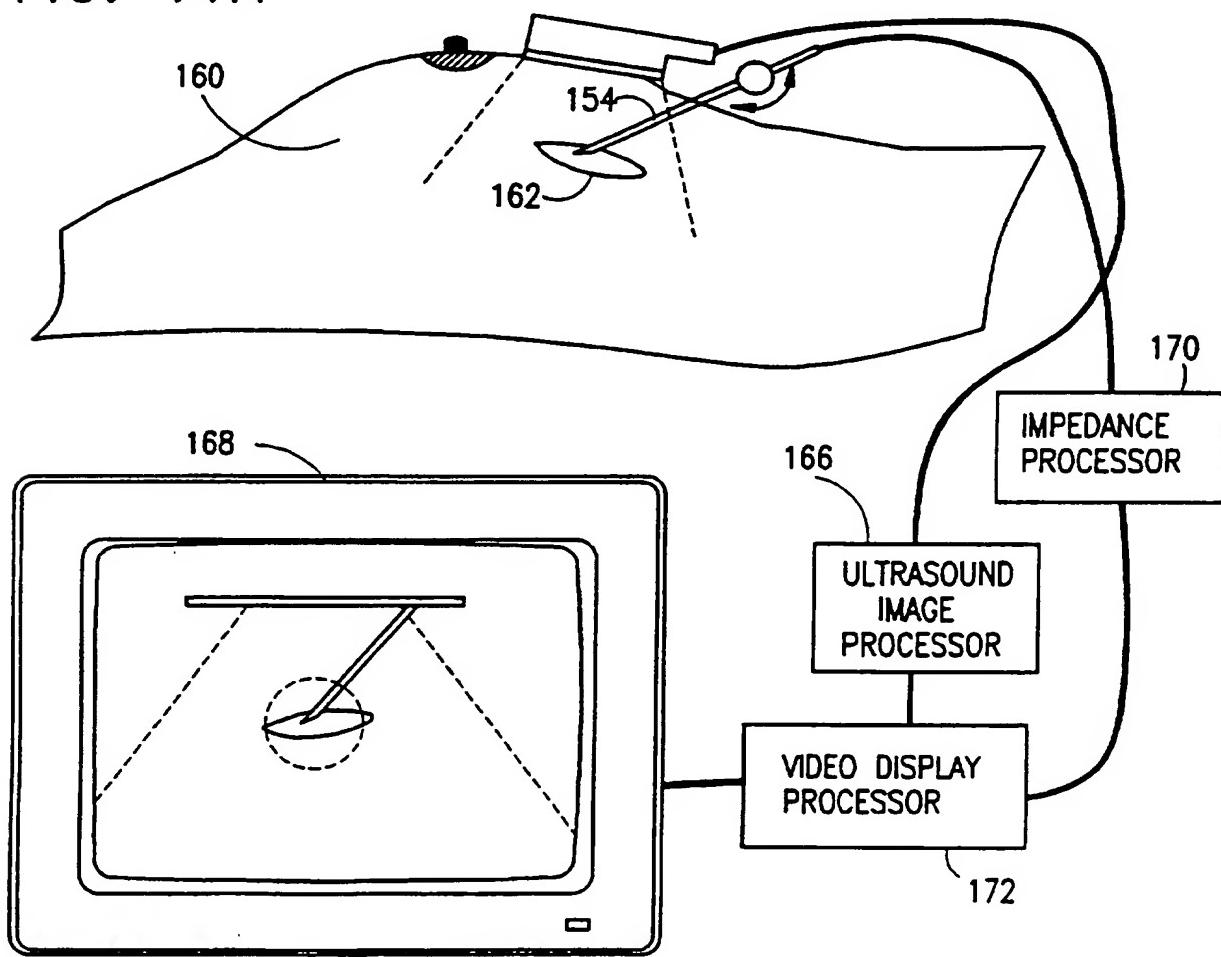
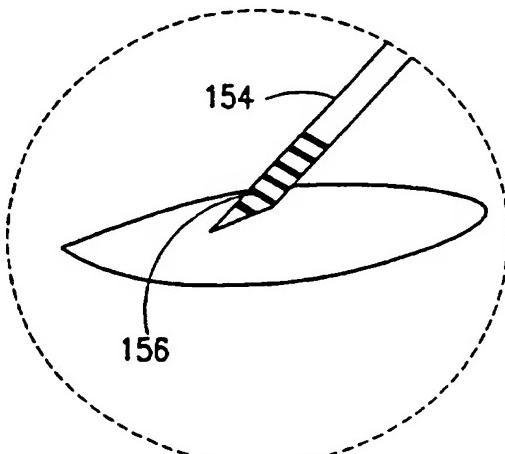


FIG. 11B



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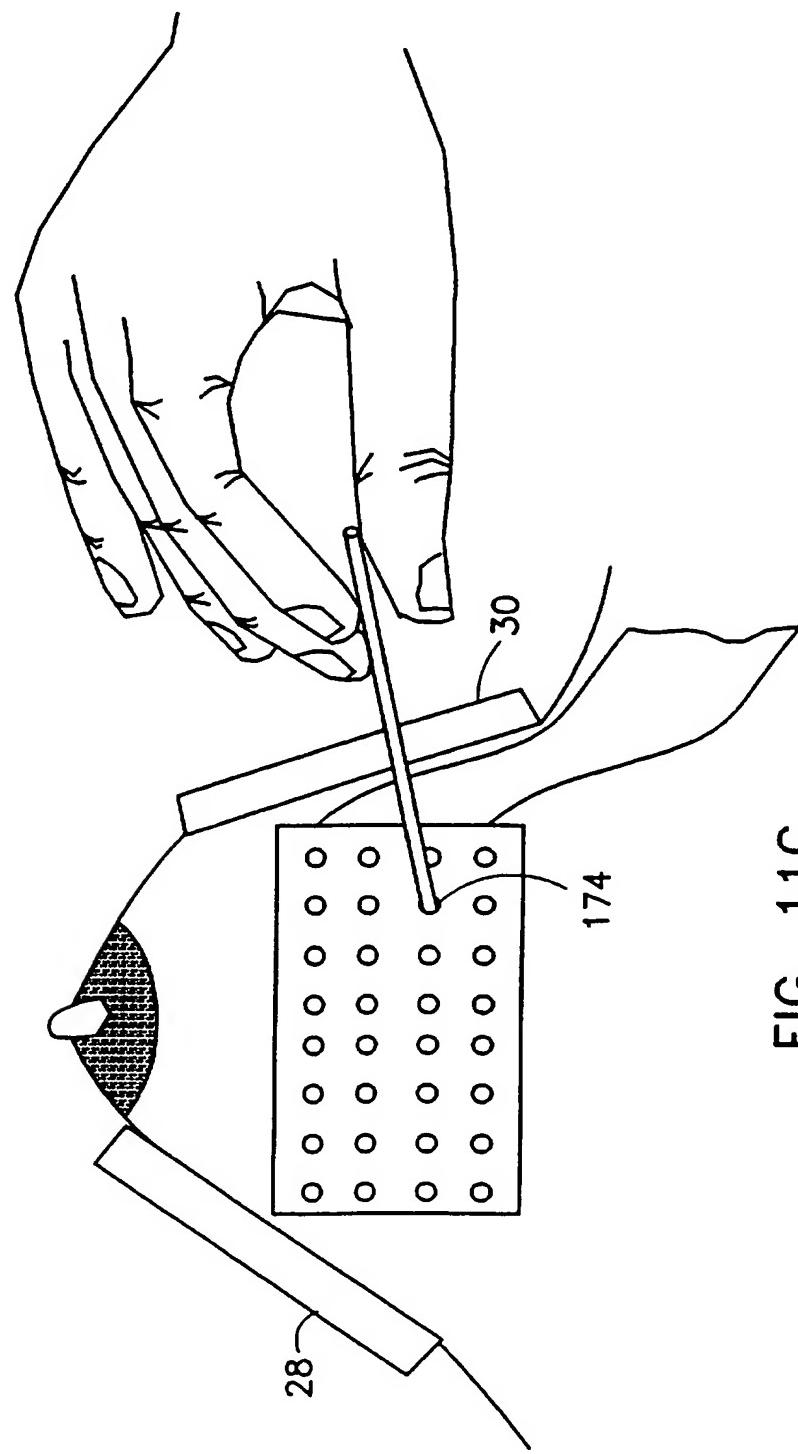


FIG. 11C

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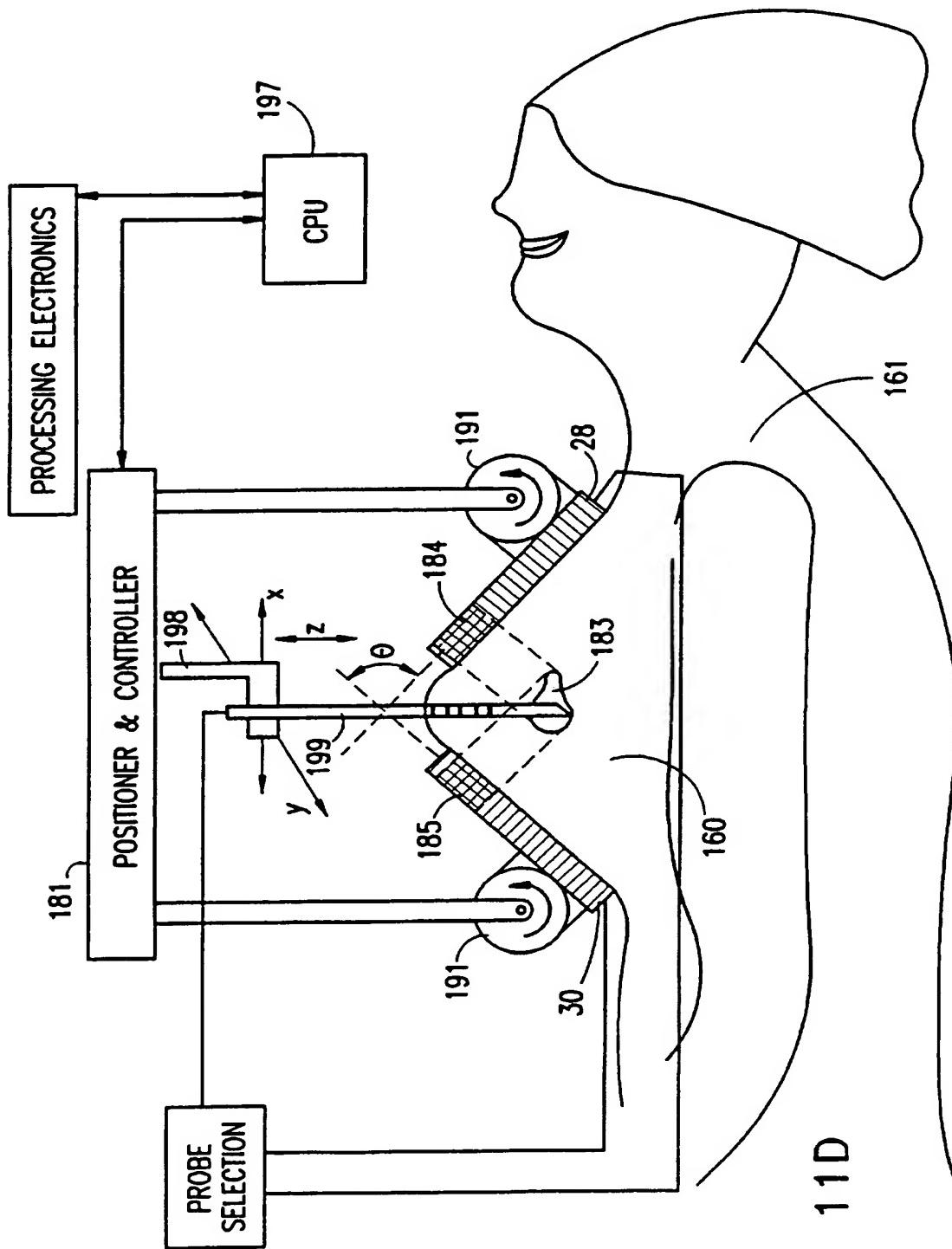


FIG. 11D

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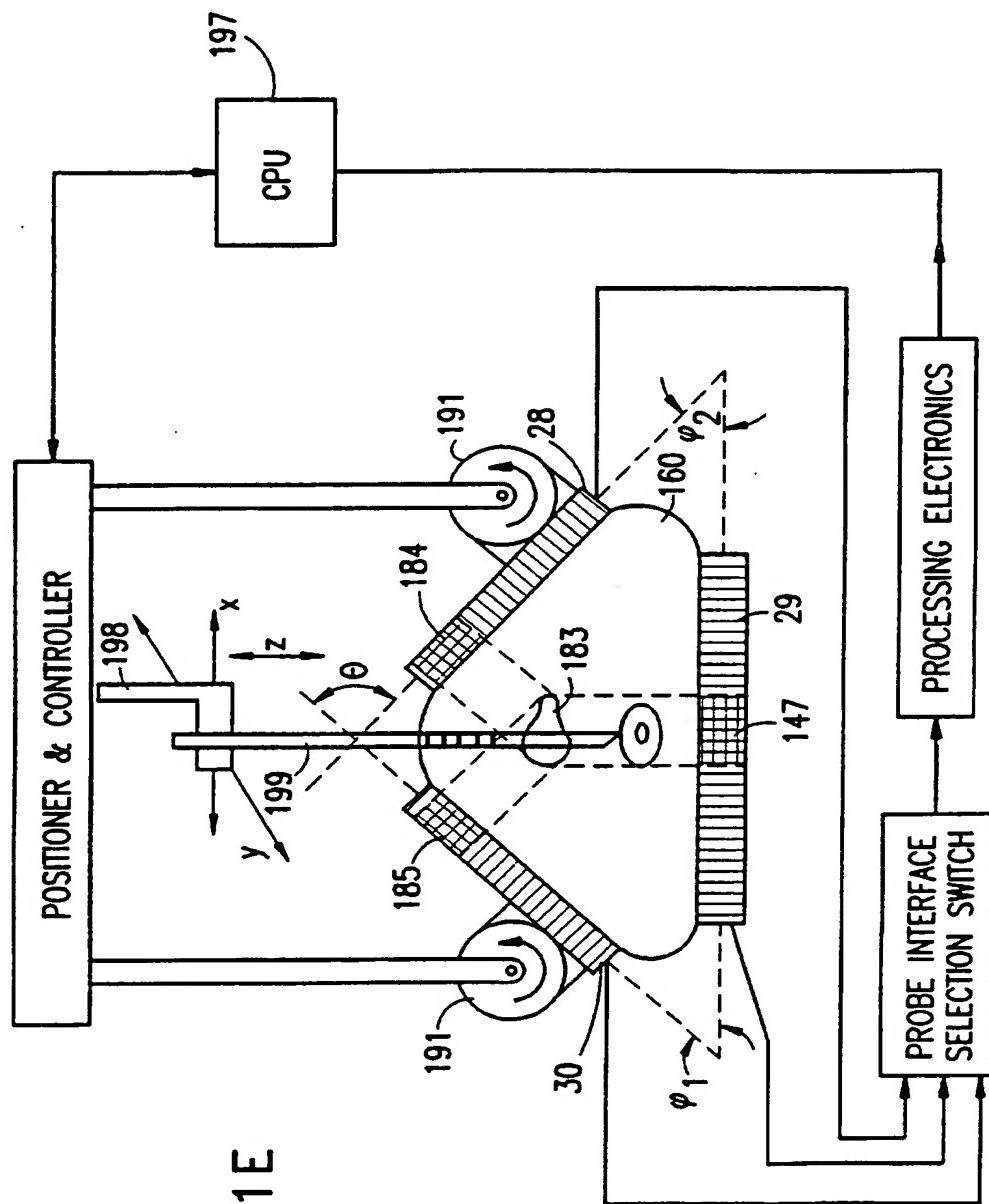


FIG. 11E

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FIG. 12

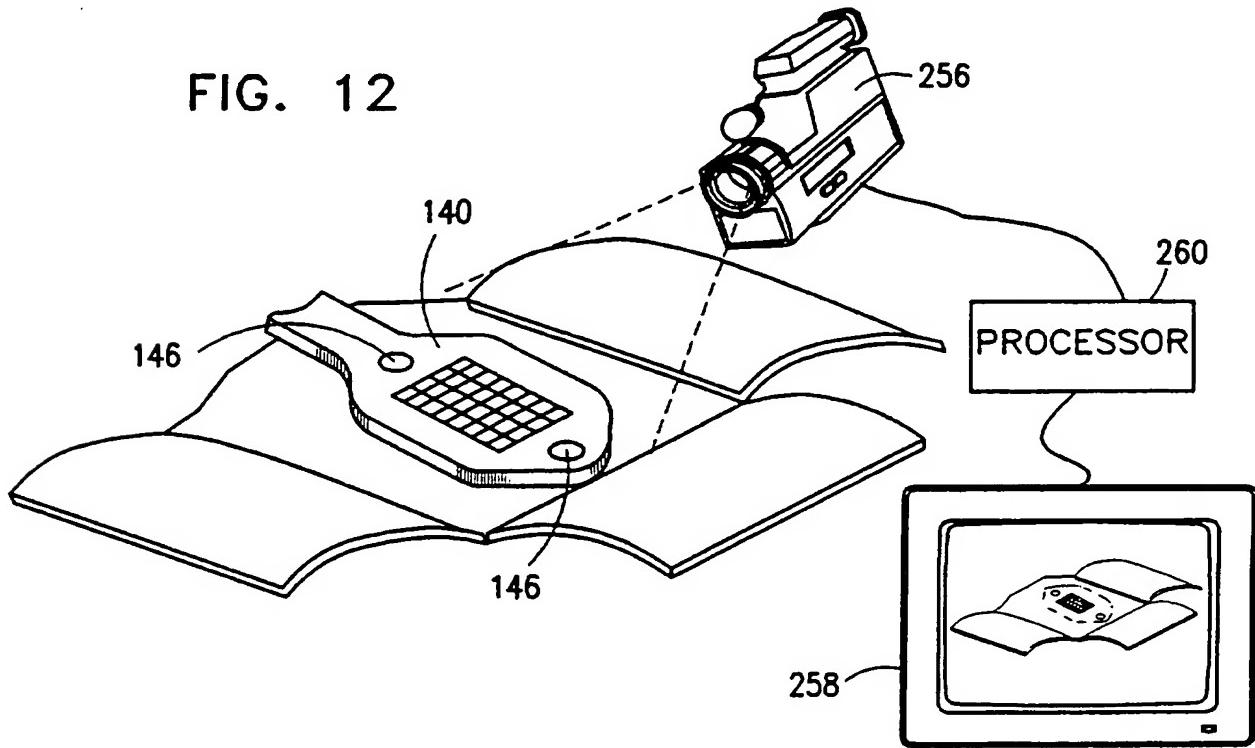
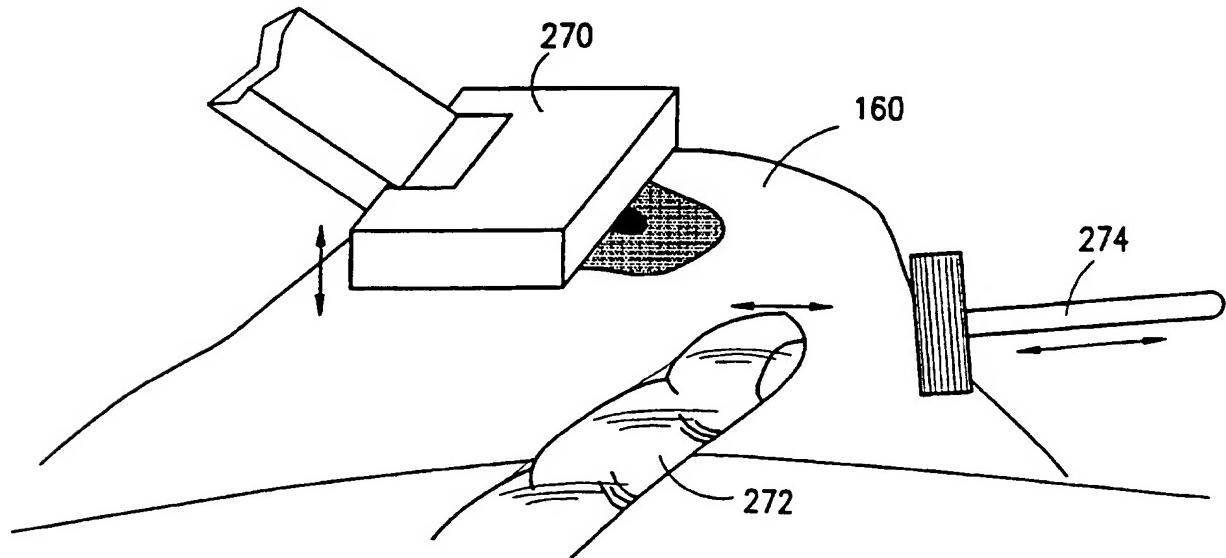


FIG. 16



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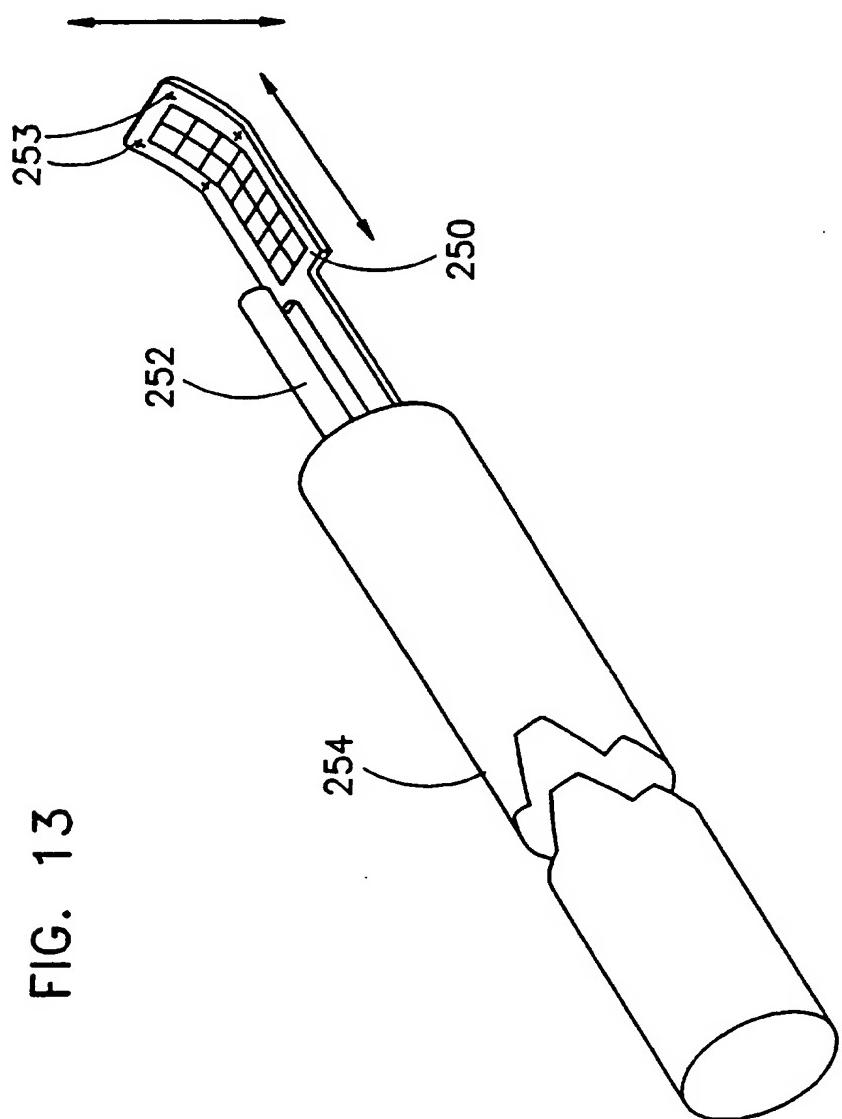
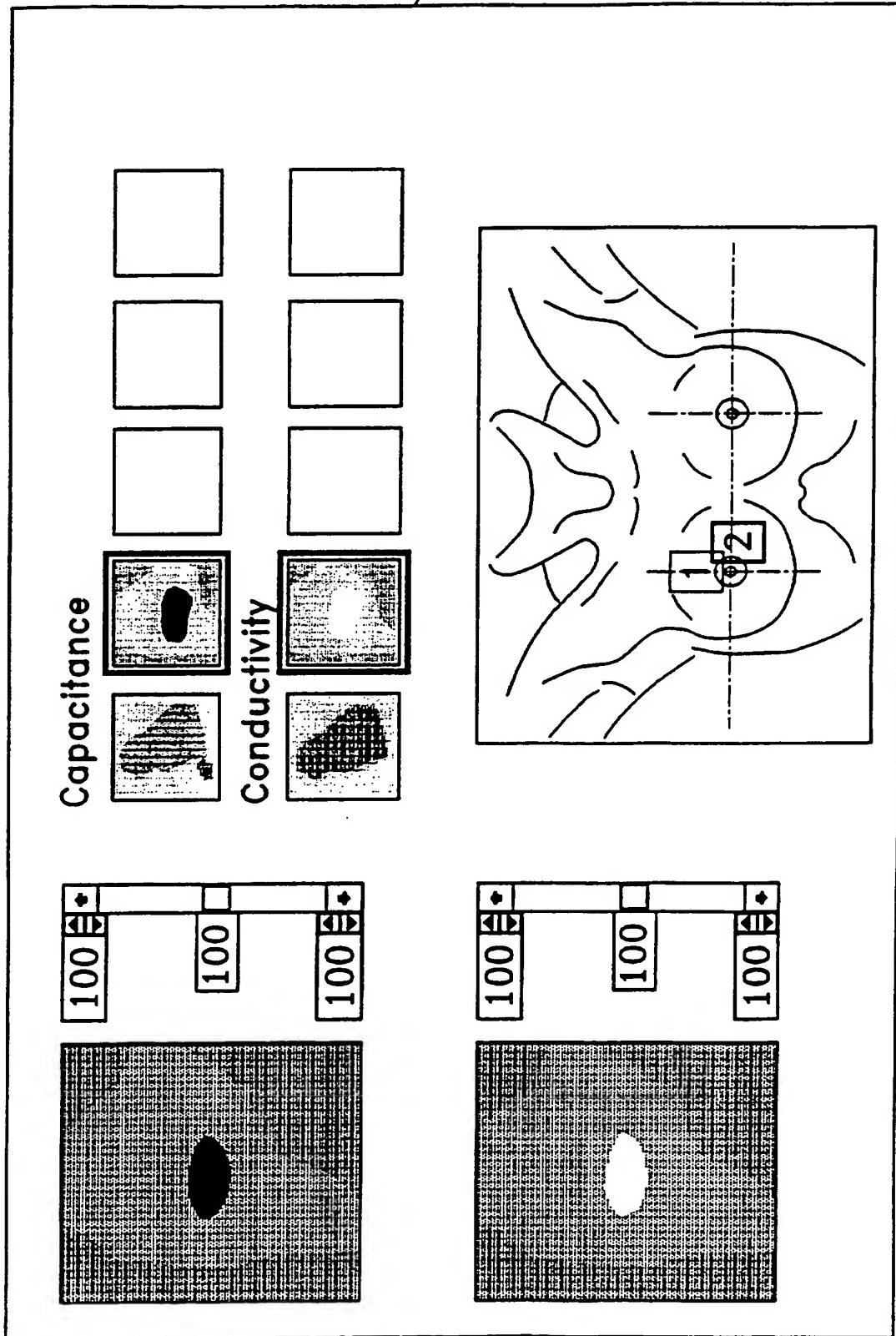


FIG. 13

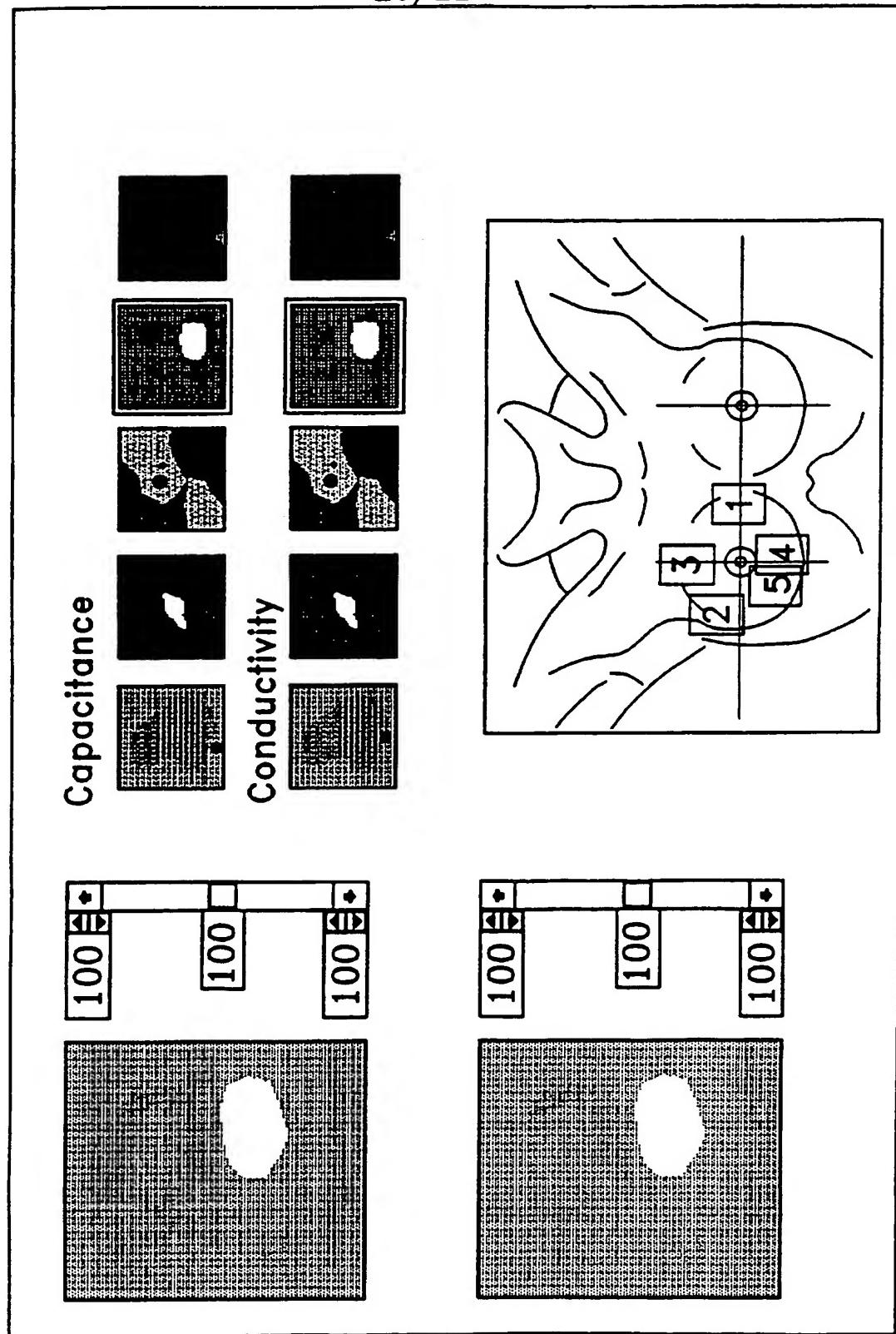
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FIG. 14



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FIG. 15



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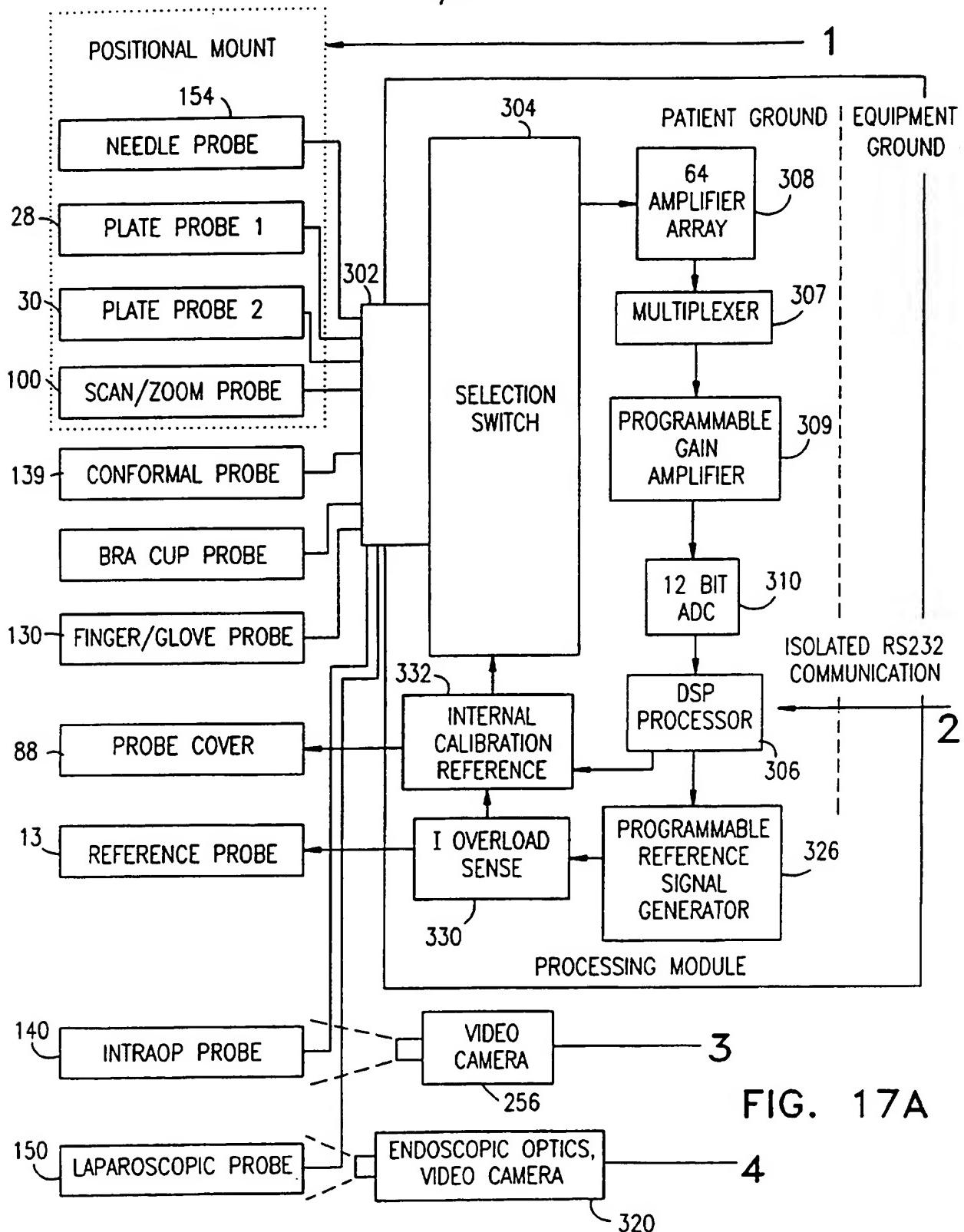


FIG. 17A

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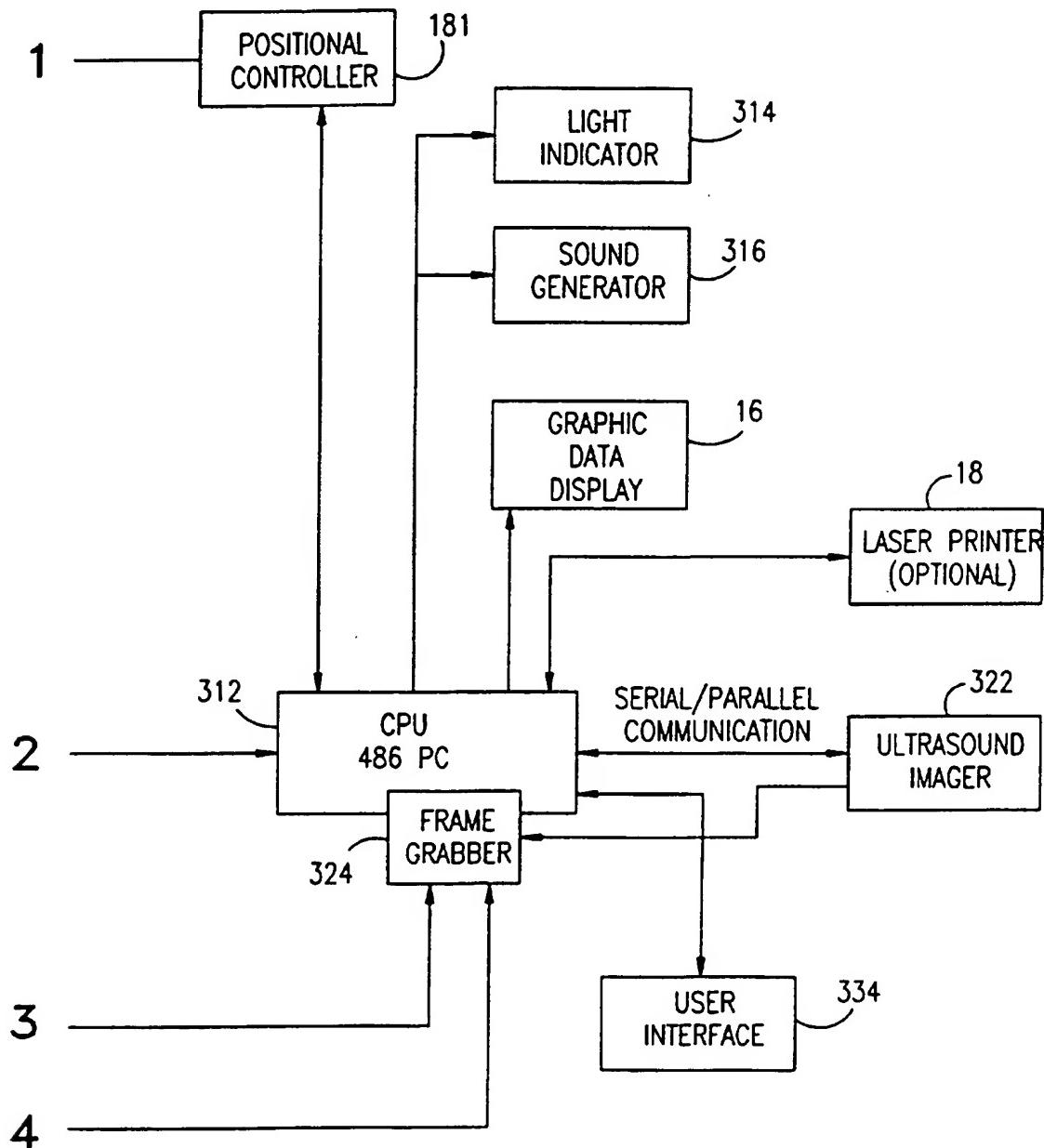


FIG. 17B

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US95/06141

A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) : A61B 5/05
US CL : 128/734

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 128/639, 640, 644, 653.1, 660.01, 660.10, 734, 736

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

NONE

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

NONE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US, A, 5,143,079 (FREI ET AL.) 01 September 1992, see entire document.	1, 5-8, 11, 14-24, 30, 32-35, 37-40, 43-56, 58-62, 68, 70-73, 76, 77
A	US, A, 4,819,658 (KOLODNER) 11 April 1989, see entire document.	1-82
A	US, A, 5,178,147 (OPHIR ET AL.) 12 January 1993, see entire document.	1-82

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Date of the actual completion of the international search 21 JULY 1995	Date of mailing of the international search report 07AUG 1995
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